Nanotechnology is the next revolution in our daily lives, which is already under way, with its amazing applications in electronics, biology, physics, materials and engineering. The book explains the basics of the new technology, its historical development, and the ongoing advances, including the pioneering work done in India. This is a non-technical preview of the wide range of applications based on nanomaterials, especially in detecting genetic defects as well as the concerns expressed on the potential negative impact of the new technology on society and its possible use by terrorists.

I welcome this book written for the lay reader by an eminent science communicator. He has provided an excellent introduction to the subject and a balanced presentation. I hope the book will motivate young people to take up nanoscience and nanotechnology for study.

C.N.R. Rao
Linus Pauling Professor and Honorary President
Jawaharlal Nehru Centre for Advanced Scientific Research

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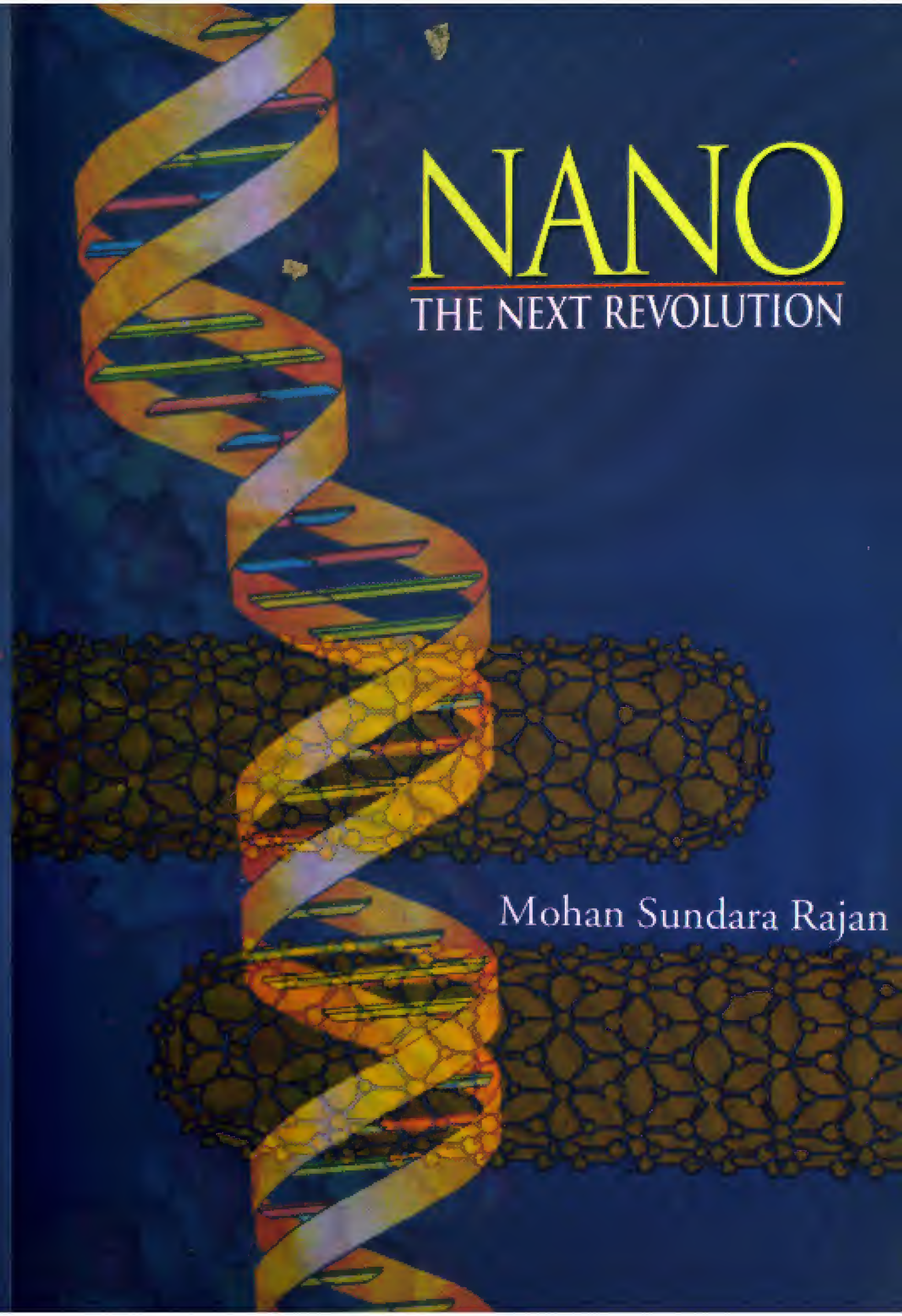

NANO
THE NEXT REVOLUTION

Mohan Sundara Rajan

NANO
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Popular Science

NANO
THE NEXT REVOLUTION

Mohan Sundara Rajan

Illustrator
Narendra Tyagi

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Foreword

There has been an explosive growth of nanoscience and technology in the last few years, primarily because of the availability of new strategies for the synthesis of nanomaterials as well as new tools for characterisation and manipulation. The subject of nanomaterials is of great vitality and offers immense opportunities. It is interdisciplinary and encompasses chemistry, physics, biology, materials and engineering. Several advanced countries have made considerable investments for promoting research and development in nanoscience and technology.

Interaction among scientists of different backgrounds will undoubtedly create new materials with unforeseen technological possibilities. Nanotechnology is likely to benefit not only the electronics and chemical industries, but also dramatically improve the quality of diagnosis of diseases, drug delivery and health care. In short, there can be hardly any aspect of our lives that nanotechnology would not change in the years to come. It is truely the next revolution in the history of technology.

In India, the Department of Science and Technology has recently launched a national initiative in nanomaterials. The Jawaharlal Nehru Centre for Advanced Scientific Research and the Indian Institute of Science, Bangalore, have been involved in nanoscience research for some time. There are many other centres in the country which have embarked on nanoscience research. These include NCL, Pune; IACS,

Kolkata; Saha Institute, Kolkata; and the Delhi University.

Even as the benefits of nanotechnology are being explored, there is concern in some countries that it may prove harmful to human health and welfare. It is therefore necessary for the public and the media to know the facts of this revolution and get a balanced picture.

I, therefore, welcome this book, written for the lay reader. The author, an eminent science communicator, has provided an excellent introduction to the subject bringing out the potential benefits as well as the concerns about its applications, illustrating the trends with examples of the work done in India and abroad in this field.

I trust that the balanced presentation in this book will motivate young people to take up nanoscience and nanotechnology for study. We just cannot afford to lag behind other countries in mastering this emerging science and technology for the benefit of our people.

I congratulate the author and the National Book Trust, India on bringing out this highly readable and timely publication.

Bangalore

C.N.R. RAO
Linus Pauling Professor and Honorary President
Jawaharlal Nehru Centre for Advanced Scientific Research

Preface

Nanotechnology will be the future with nanoscience developing nanomaterials and devices. This will lead to further convergence of technology with wide applications.

—President Dr A.P.J. Abdul Kalam

Nanotechnology, emphasised by our respected President, poses a challenge to our younger generation to think of innovative ways of making the world a better place to live in without fear and want. This book is an attempt to enable our younger generation to understand and appreciate a technology that is bound to affect them profoundly when they grow up and motivate them to apply it for the benefit of our country.

For the first time in history, humans have acquired the ability to see and manipulate matter at the scale of a nanometre (billionth of a metre). Nanotechnology, which makes this possible, is emerging as the all-embracing innovation triggering the next revolution in our daily lives and the materials we handle. The impact of the revolution is expected to be on almost all aspects of our daily life with the promise of finding a solution to many of the pressing problems of the world.

The book describes the concept of nanotechnology, traces its origin and subsequent developments and outlines the scope of its applications. Beginning with an

Acknowledgements

I am grateful to Prof. C.N.R. Rao, distinguished scientist, Linus Pauling Professor and Honorary President of the Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore for his encouragement and guidance.

My special thanks are due to his colleagues, Prof. G.U. Kulkarni and Dr A. Govindaraj for clarifying numerous technical points relating to nanoscience and technology. I thank Prof. D.D. Sarma of the Solid State and Structural Chemistry Unit of the Indian Institute of Science, Bangalore, and his colleague, Mr Sameer for their helpful suggestions and comments. I thank Prof. A.K. Sood of the Physics Department and Prof. K. Chattopadhyay of the Department of Metallurgy of the same Institute for their comments. I thank Dr Murali Sastry of the Materials Chemistry Division, NCL, Pune for sending comments on the work of his group.

My special thanks are due to the Jawaharlal Nehru Centre for Advanced Scientific Research, the SSCU and the Physics Department of the Indian Instititute of Science as well as Intel (and its media coordinator, Mr Vishak Gopinath of 20:20 Media), for providing visuals for the book.

I thank the German Embassy in Delhi for permission to use a quotation from an article in *German News* on the contribution of S.N. Bose and Einstein.

I also thank National Book Trust, India for their contribution in bringing out the book.

THE AUTHOR

1

WHERE SMALL IS BIG

To understand the very large, we must understand the very small.

—Democritus (400 BC)

Nano, the Greek word for 'dwarf', indicates one billionth of something. A nanometre (nm) is a billionth of a metre. It is 100,000th the diameter of a human hair. Each nanometre is only three to five atoms wide. The period at the end of this sentence can take five million carbon atoms!

Nanotechnology refers to the technology of rearranging and processing of atoms and molecules to fabricate materials to nano specifications such as a nanometre. The technology will enable scientists and engineers to see and manipulate matter at the molecular level, atom by atom, create new structures with fundamentally new molecular organisation and exploit the novel properties at that scale. Matter at the nanoscale is different from its bulk form; its chemical, biological, electrical, magnetic and other properties are different from the properties of macromatter. As a result, faster, cheaper and better products would emerge.

The realm of nanotechnology lies between 1 and 100nm. The diameter of one hydrogen atom is 0.1 nm. The width of a DNA molecule is 2.5 nm. Glucose is just below 1 nm in size. Several polymers and some particles measure up to 100 nm. In contrast, biological cells are on the micrometre

scale (millionth of a metre). But one thousand bacteria could be placed in 1 nm.

There is no one interpretation of nanotechnology acceptable to all. The term, however, generally refers to the creation and use of objects and structures that are at least in one dimension 1–100 nm in diameter. The term also denotes processes that control the physical, chemical or electronic attributes of such materials. Another definition mirrors Nature's art of 'building up' by self-assembly atoms and molecules into useful structures. Nanosystems are different from the currently known micro electromechanical systems (MEMS), which refer to machines with moving parts smaller than a human hair and that contain both electrical and mechanical components.

It is known that all things are made from atoms. The properties of materials depend on how their atoms are arranged at the nanoscale. If only the atoms of an object are rearranged, then a new object would emerge. However, atoms cannot be easily handled. It is like fixing the small pieces of a picture puzzle with boxing gloves on. If we have the right tools to get every atom in the right place, we could make almost any structure consistent with the laws of nature. This is technically known as positional assembly. Nanotechnology is based on the ability to explore objects at the nanoscale and manipulate them wherever possible.

Materials and devices, designed and made at the molecular level, would be quite different from those in daily use today. The new products would be far superior in terms of strength, toughness, speed and efficiency. Though most of the processes are in the experimental stage, commercial ventures have already come up with projects to exploit the potential of high quality and low cost of materials based on the new technology. It is interesting to note that nanotechnology is set to bring about a fundamental change in several areas—materials science, electronics, biology,

medicine—and is expected to profoundly change the pattern and standard of life of people worldwide. In short, it would be true to say that the small would be really big!

The emerging world of nanotechnology comes in the wake of major changes in the use of technology. However, the pace of change in technology, which essentially depended on basic materials, has been very slow in the Stone Age but picked up a little in the Bronze and Iron Ages. In contrast, the changes gained momentum from the Chemical Age around AD 1900. Subsequent progress was rapid and complex in the Plastics Age (1940s), the Materials Age (1960s), the Silicon Age (1970s), the Biotechnology Age (1980s) and the Genomics and Information Age (1990s) (Fig. 1.1).

Right from the Middle Ages, the urge to probe matter and manipulate it in search of the proverbial gold has been punctuated by philosophical contemplation on the nature of matter and its constituents. Some of the theoretical

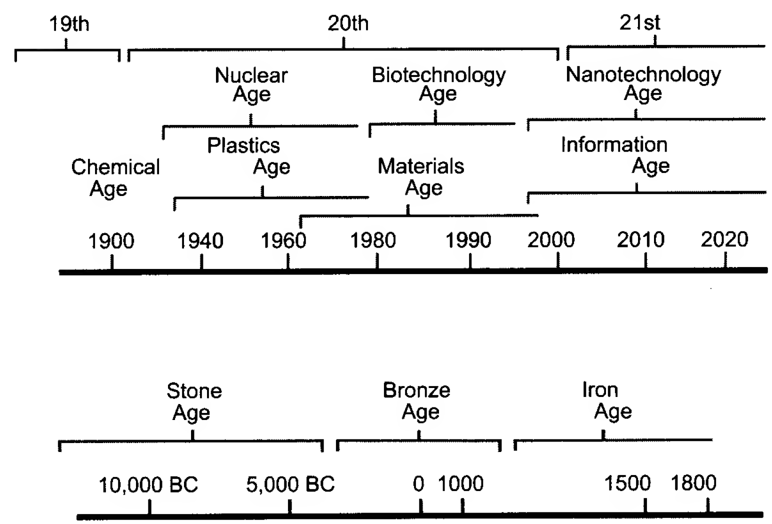


Fig. 1.1: From Stone Age to Nano Age: Progress of Technology.

predictions have been eventually verified with the advent of modern instruments. The ongoing Information Age is noted for outstanding advances in the biological sciences as well. Biologists and information scientists have joined hands in exploring matter at the nanoscale and have discovered new features of many materials. An interdisciplinary study with revolutionary implications for the entire world is emerging. The study of nanotechnology and its applications is expected to dominate the 21st century.

Hailed as the all-embracing innovation of the 21st century, nanotechnology is expected to impact on almost all aspects of life. Nanotechnology is an enabling technology, as it would impact on almost every area of research. Research at the nanoscale is bringing together chemists, physicists, chemical engineers as well as computer experts, biologists and doctors in a truly interdisciplinary manner. The results of this endeavour are likely to affect almost every aspect of our daily life. The impact is expected to be global and will be visible in the nature of food, clothing, shelter, transport, communications, drugs, disease detection and prevention and innovative treatment. Nanotechnology will rediscover our immune system, our genetic make-up, reinvent and reengineer industrial production and rewrite the strategy of war. Nanotechnology is designed to bring out an entirely new generation of products, cleaner, stronger, lighter and environmentally friendly. On the down side, nanotechnology might become too dangerous for widespread use and may well become a deadly weapon in the hands of terrorists. Even otherwise, the nanorevolution could spell the end of human control over matter.

In the last two decades path-breaking discoveries and inventions of new microscopes have led to a lot of hype in the media about the ability of nanotechnology, which has inevitably triggered equally unrealistic negative reaction and scare stories centred on terrorists. An overview that

separates the science from the fiction in this matter is urgently called for. Moreover, a knowledge of the challenges met and the results achieved is essential, if the younger generation in developing countries, such as India were to acquire an interest in the new field of nanotechnology and become motivated to address the challenge of applying it for the benefit of their people. India has taken the initiative to encourage research and application of nanotechnology. And selected scientific establishments in the country have done outstanding work in this field.

The world of nanotechnology can be subdivided into two major application areas: the wet and dry areas. Nobel Laureate Richard Smalley has described the applications in the two areas. According to him, the wet area includes the biological domain, where nanostructures may function within biological cells. The area includes dendrimers, round-shaped molecules that branch out again and again forming spherical blobs. The dry area consists of what is called hydrophobic (water repellant) architectures and strategies that govern improvement of materials including computer chips. Dry nanotechnology applications have preceded the biological usage.

It is a happy coincidence that the exploration of the nanoworld has come at a time when computers have become amazingly powerful. The next generation of supercomputers will have more than a *million* processors each capable of a *billion* operations per second. Such power would be useful, among other applications, in exploring complex phenomena at the nanolevel such as protein-folding inside the human body. Computer modelling would become more and more realistic and help choose the best possible leads in research.

Equally fascinating is the increasing use of a new generation of microscopes to probe matter at its most basic level, which can never be seen by the naked eye. The atomic force

microscope, for instance, does not use light but measures the force between atoms in a sample, resulting in high resolution in imaging molecules such as proteins. The tip of this microscope is smaller than most viruses. The minimum feature in an integrated circuit is 0.1 micrometre (in 2002), which is indeed smaller than cells or bacteria.

New Horizons of Discovery

The new class of microscopes has led to an amazing discovery: the very properties of matter depend on its size. The nature of matter on a nanoscale is dramatically different from its bulk form. Its optical and electrical properties and even colour change. New horizons of discovery, based on this feature, are emerging.

The new-found ability to see and manipulate molecules has enabled scientists to emulate nature by building materials from simple atomic level constituents, instead of from the *top down*. If only one can put atoms where one wishes, one can work wonders in constructing new forms of matter. However, this is not what happens today. Exactly the opposite method, known as *top down* approach, is followed in areas such as chip making. The new approach is now coming into use. Transistors will be built *bottom up* from individual molecules as against the current practice of chopping bigger pieces of matter into smaller units.

Nanotechnology poses a challenge to manipulate atoms individually and place them precisely where they are needed with pre-defined features. Traditional manufacturing methods such as casting and welding, place atoms randomly. Even with precise tools, exact positioning of atoms is not possible, though a good deal of precision is in fact followed in a macroscopic manufacturing system. Chemical synthesis alone can create molecules with exactly defined atomic composition and geometric structure. Besides chemical synthesis, assembly of nano objects has become important. 'Soft' chemical approaches have become popular in assembling nano objects. The soft approach is based on mild reactions rather than on brute force in evolving new chemical materials.

Today's nano devices can generally be placed where computers were in the late 1950s. The remarkable progress in computer sophistication and power has reduced their size from being a roomful to a laptop. Some of the key innovations such as the World Wide Web have brought the benefits of the Internet to common people everywhere. Similarly, nanotechnology too is expected to bring about fundamental improvements in several areas. While the Internet has turned into reality the extraordinary facility of connecting anyone, anytime, anywhere; nanotechnology is poised to endow ordinary devices and techniques with extraordinary powers. Moreover, self-replicating assemblers are expected to rebuild almost anything, though this is now being described as a long-term aim.

Initially, biology and electronics are likely to be the major areas of application. Nanotechnology is expected to provide a new tool to read the genetic code. Cancer, for example, can be detected at its very early stages, even when only a few cells are affected, invisible with today's technology. And nanoscale robots (called 'nanobots') would be released into the bloodstream programmed to image the affected areas and later on to deliver drugs.

In the field of electronics, nanotechnology is expected to bring about further miniaturisation in numerous devices as the circuit reduction now being made approaches the limit of the resolution set by the physics of light diffraction.

Other applications cover a wide field, ranging from novel materials to anti-terrorist devices. Some nano products may go into commercial production in the next five years. Such applications have to await a full understanding of the behaviour of different materials on a nanoscale.

Unexpected areas of application would come, when nano electronic devices effectively interact with one another or with living matter. After the initial bout of hype about the applications, a sober reappraisal has set in separating the practical possibilities from science fiction about nanotechnology.

There are three major risks in entering the nano world. One is posed by terrorists who may deliberately or unwittingly let loose some of the nano weapons being developed with no means to alter the outcome. Another risk is rather subtle and arises from the steady domination of nano robots in everyday life, which will make human intervention difficult, if not impossible. The third risk is the most subtle and yet the most dangerous. It is the hazard posed to human life and health by nanoparticles inhaled in the factory and elsewhere. There is growing concern about this risk and several studies are under way. The jury is still out on this issue.

2

MICROSCOPES WITH A DIFFERENCE

The deepest sin against the human mind is to believe things without evidence.

—Thomas Huxley

Progress in Western science and technology, especially between AD 1200 and 1700, is sometimes attributed to the development of glass. It is interesting to note that spectacles for reading were available only from the 13th century. It was in the 17th century that a Dutch spectacle-maker, Hans Lippershey, succeeded in making the first telescope as well as a microscope. While telescopes were made bigger and better in subsequent years, the development of the microscope lagged behind. It was only in 1665 that Robert Hooke in England conducted experiments with a microscope and published what he saw in cells and bacteria.

It was soon realised that the laws of physics impose a limit on optical microscopes. The crests in a wave of light are about 500 nanometres apart. Traditional optical microscopes cannot resolve objects that are smaller than about half the wavelength of light. Hence, the search began to use electrons or X-rays to increase the spatial resolution of objects. The innovations that followed resulted in new kinds of microscopes that have revealed the nanoworld within living beings.

By the 1930s, the control of electron beams in vacuum had matured. This resulted in the development of

transmission electron microscope (TEM) using magnetic analogues to lenses. Ernst Ruska, an engineer at Technical University of Berlin, invented it in 1933. In TEM, a focused electron beam sent to the specimen interacts with it and the data show the composition of the specimen. The idea of such a microscope was based on a proposal made by Prince Louis de Broglie, a French theorist, in 1924. He held that electrons, though traditionally imagined as particles, can at times behave like waves. The idea did not gain ready acceptance. It took almost ten years for the idea to be realised through an electron microscope.

Ruska and his team focused their microscope on electron waves. The scientists used several electromagnetic equivalents of lenses. The energy of the electrons was increased so that the wavelength was 1,00,000 times shorter than that of light. The electrons that had interacted with a specimen were photographed to get a magnified image. A TEM could, for instance, observe catalysts in action instead of the reactions either before or after the catalysts come into play. As the electron beams interact with a specimen, a rich variety of signals are produced, yielding information on the composition of a specimen. In short, matter could be seen at the atomic scale.

By the end of the 1960s, electron microscopes could magnify several million times. The structure of cells and even individual molecules and catalysts in action could be seen. TEM is now a powerful tool of research in chemistry used in many countries including India.

Scanning Tunnelling Microscope

The next major advance in microscopy is the scanning tunnelling microscope (STM), which gave stunning insights into the world of single atoms. It was invented by Gerd Binnig and Heinrich Rohrer of IBM's Zurich Laboratory in 1981. It became possible to image individual atoms by scanning over

the surface of a silicon crystal and study structures and processes at the atomic scale. Soon it was easy to image individual atoms. STM uses a fine-tipped needle, which consists of only a single atom. It is made to move over a surface, contracting and expanding by very minute amounts. As the tip nears the sample's surface, its electrons 'tunnel' between the sample and the tip. And as the electrons scatter off the successive target points, a contour map of the surface emerges. The resulting image shows cross-sectional details at the scale of individual atoms. The scientists who invented the STM and TEM won the Nobel Prize in 1986. Following the invention, the Nobel Committee said, 'It is clear that entirely new fields are opening up for the study of the structure of matter' (Fig. 2.1).

By 1988, it was possible to move atoms and molecules around in a planned manner. An IBM researcher, Don Eigler, used a STM in 1990 in an interesting experiment. His team 'moved' 35 xenon atoms to sub-nanometric precision to display the company's trademark 'IBM'. The atoms stood out prominently. The display convinced scientists that atoms could easily be manipulated.

STM was also used (in 2002) for measuring magnetism at the atomic scale. Scientists believe that a magnetic spin of a material could be used to develop faster and smaller electronic devices. It is expected that

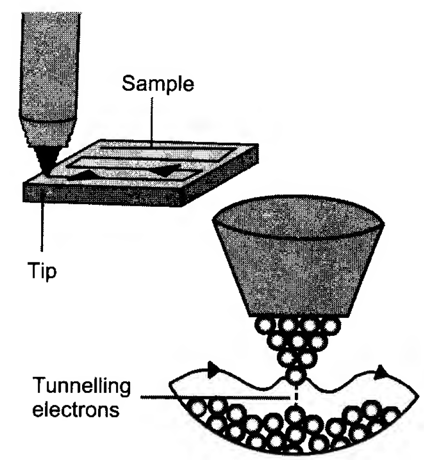


Fig. 2.1: Scanning Tunnelling Microscope. As it scans the surface of a sample from a distance, the electrons tunnel between the tip and the surface and produce an image of the sample.

the technique would be useful in the production of more powerful hard drives and other devices. The STM proved to be ideal for measuring the tiny force between nano devices in a vacuum.

Atomic Force Microscope

It was soon realised that electron beams could be controlled only in a vacuum. Hence, it could be used for viewing only non-living samples. Biological processes such as breathing could not be observed through it. This led Binnig and his colleague to invent yet another type of microscope, known as the atomic force microscope (AFM) in 1986. It is essentially based on measuring the force between atoms. AFM provides significant advantages as an imaging tool compared with electron microscopes for making topographic maps of nanostructures including biological samples in real time. It has an externally visible ultra-sharp tip (with a radius of 20 nm), which resembles a gramophone needle. It touches the sample with a force of one-tenth of a millionth of a gram. It can also tap across the surface. As the tip is either attracted or repelled, the cantilever to which the probing needle is attached, bends. The deflection of the sensitive cantilever is measured using a laser beam. No constant distance is maintained between the tip and the sample. A computer records the path of the tip and slowly builds up a 3-D image. The surface of the sample can be measured at nanometre or even subnanometre level, better than 1 nm laterally and 0.01 nm in height. It can also be used to map surfaces of a range of objects from computer chips to deoxyribonucleic acid (DNA). AFM provides molecular resolution even when the sample is in a fluid in real time. Moreover, the tip of the AFM can move molecules around on a surface. An AFM can also make indentions on materials, unlike an STM that only images samples which have electrical conductivity (Fig. 2.2).

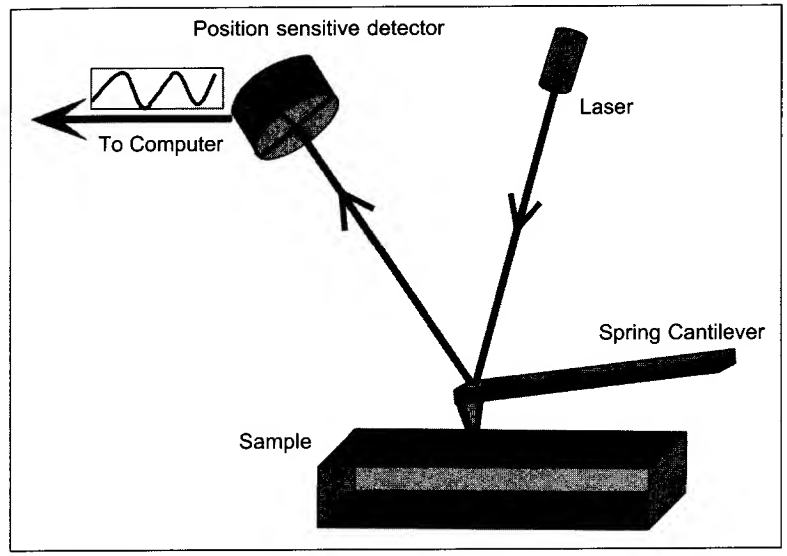


Fig. 2.2: Atomic Force Microscope. It records the force felt by its cantilever as the sharp tip is brought close to–or even indented into–the surface of the sample and then pulled away. With added instruments, the microscope can produce images in a number of other modes as well as provide data on the magnetic force or electrical force of the sample. The microscope is applicable to both conducting and insulating materials.

An AFM can measure nano forces too. A prototype device has been developed to measure the nano Newton force, which is one billion times smaller than the force needed to hold an apple on the Earth! The nano force, for example, is involved in pulling apart a molecule.

Prof. John Pethica of Oxford University developed a new kind of AFM, which allows direct imaging of force gradients and some features of chemical bonds. In fact, he had outlined the concept of forces acting between the tip of a scanning tunneling microscope and the sample's surface.

A modified AFM was soon developed with a nanotip instead of the conventional silicon tip. The new device used a carbon nanotube—just a nanometer across. It would be useful in experiments designed to detect genetic variations

that account for various diseases (*see* Chapter 7). The device not only traces a sample's surface but also helps make a very slight impact on it, some 20 trillionths of a metre. The feature is particularly useful in measuring the mechanical properties of soft materials or hard material in liquid. For instance, scientists have measured for the first time the hardness and elasticity of matter at the junction between tooth enamel and dentin, which is 50 per cent mineral, 30 per cent organic material (collagen) and 20 per cent fluid. Collagen is the most abundant animal protein that holds the bones and tendons together. With a modified AFM, one could measure hardness to a depth of less than 20 nm. This feature is also useful in interpreting seismic data.

AFMs only work when they touch the surface of a sample. Hence, they cannot be used where it is hard to reach. Scientists have tried an ingenious way to overcome this problem. It has been found that kinesins that carry molecules to cells latch on to rod-like proteins called microtubules, tagged with fluorescent markers. The glowing proteins are photographed every five seconds. The technique can be used to check the presence of a chemical.

An AFM tip can act as a pen to 'draw' with molecules as 'ink'. It can pick up different types of molecules and put them on a substrate. The process is known as dip-pen lithography.

AFM images contain less information than those revealed through the traditional X-ray diffraction techniques; but the image can be captured in minutes. In contrast, much longer time is needed in the X-ray diffraction technique.

Scanning probe microscopes (STM, AFM and their variants) are becoming standard equipment in laboratories around the world. Some industrial establishments too have them for quality control. The AFM at the Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore, is called 'Conducting AFM'. It is one of the six such facilities in the world. The microscope can not only measure the

topography of a surface in the nanoscale but also map its electrical conductivity.

Without the scanning probe microscopes, scientists would not have been able to explore the nanoworld. The devices have enabled biologists to look at DNA and molecular processes. The devices have become as crucial for nanotechnology as the printing press was to communication.

Raman Spectroscopy

Another remarkable technique to probe matter at the molecular level is Raman spectroscopy, based on the insight provided by the celebrated Indian physicist and Nobel laureate, C.V. Raman (1888–1970). He showed that visible light has particle-like properties. He pointed out that the blue colour of the sea was not because of its reflection of the blue sky but due to the scattering of light by the molecules of water. Spectroscopic analysis is based on the change of frequency in the scattering of radiation in a medium.

In 1928, he discovered a new technique to probe the structure and dynamics of matter. Since known as the Raman effect, the technique gave a remarkable insight into interactions of light and matter (Fig. 2.3). In the last 75 years since his discovery, the physical phenomenon of scattering of light described by him has become an important technique used in a wide variety of applications in physics, chemistry and biology. Technological advances in microscopy and related tools continue to enhance the value of Raman spectroscopy. Today, matter can be seen at a spatial resolution of a few nanometers and the Raman effect is still valid. In the early 1970s, a professor of cell biology, George J. Thomas (Missouri, Kansas city), pioneered work on the Raman spectroscopy of viruses.

In order to provide a better image of the principal structures of the sample, nanometer-size gold crystals are attached to the tip of a scanning probe in a technique called

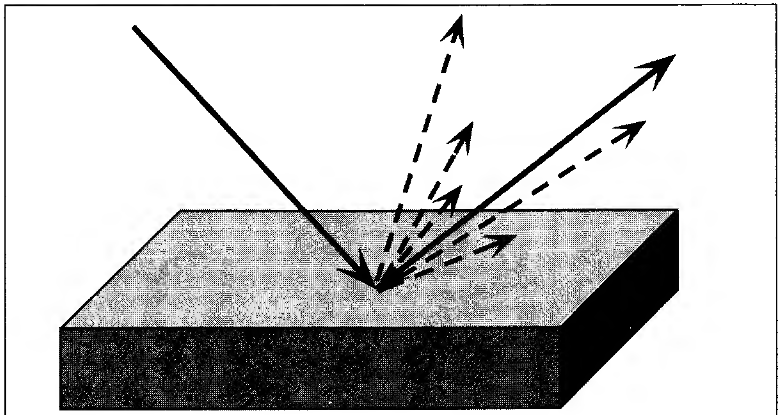


Fig. 2.3: The Raman Effect. When a laser beam is focused onto the surface of an object, most of the light is reflected off without any change. A small portion of the light, however, interacts with the molecules in the object and is scattered. The scattered light is known as the Raman effect. It is collected to produce a spectrum. Each material has a unique spectrum associated with it and can serve as its fingerprint.

surface-enhanced Raman spectroscopy. It is used to obtain spectral data from molecules and enhance the result by a *billion* times. It is claimed that the process can help detect a single molecule, which is a challenging task. The advent of laser sources since the 1960s gave a new edge to study the Raman effect. Developments in the semiconductor industry such as photodiodes reduced the time for scanning the spectrum of diffracted light.

Today, Raman Optical Activity (ROA) spectroscope has become an important tool for studying biomolecular structures such as viruses and proteins. The spectroscope, pioneered by Lawrence Barron of the University of Glasgow in 1973, can measure very small differences in the intensity of the incident laser light and the light scattered from the responding molecules. Barron pioneered the technique of

using the spectroscope to study the structure and behaviour of proteins and gained new insights into what is known as protein misfolding diseases. It has been demonstrated that light emissions from a sample could be enhanced by an ROA spectroscope a million times or more, if the sample is examined together with a metal colloid (a substance composed of ultramicroscopic particles).

A New Area of Interest

As nanotechnology is emerging to underpin a new generation of deep-probe detectors, a new area in the electromagnetic spectrum is becoming available for probing the human body as well as revealing hidden matter. The area of interest is at a frequency of about a trillion waves per second, as against millions and thousands used for short-wave and medium-wave radio propagation, respectively.

Known as terahertz radiation, the area is in between light and radio waves in the spectrum. It can pass through several solid materials and can yet be used to provide images. It can be used to see tumours within the skin, by distinguishing fat from protein and spot cavities in teeth. Increased blood supply to tumours would identify them in scans using the terahertz waves. The detectors (photonic crystals rather than glass lenses) in the terahertz camera will have many other uses, including surveillance on terrorists and airport baggage screening.

Nanotechnology would have been a pipe dream but for the special microscopes. These extraordinary probing instruments, invented in recent years, are still revealing ever-new features of the nanoworld.

3

EVER-NEW FORMS OF MATTER

The world is full of things, which are all in some form mere combinations of atoms; the forms change but the atoms remain forever.

—Kanada (Ancient Indian philosopher)

The human mind has tried to understand the material world through philosophy as well as science. In fact, the emergence of new materials and the technology based on them has marked the various ages in history. Every age has taken advantage of the progress made in the preceding age in terms of new materials and their applications. The pace of discovery and invention gathered momentum since the Renaissance in Europe in the 16th century. It is only in recent decades that humans have started acquiring the ability to see and manipulate matter at the atomic level.

Kanada and Democritus

In retrospect, two scholars, one in India and the other in Greece in ancient times stand out for their remarkable insights in understanding matter at the atomic level. One of ancient India's philosophers, Kanada (exact date unknown; could be any time between 300 BC and AD 800) held that things in the world are composed of atoms of different kind as are the various elements and that all things are just combinations of atoms. 'The forms change', he said, 'but the atoms remain indestructible'. Kanada also regarded light

and heat as variants of the same substance.

Democritus of Greece (about 400 BC) coined the word 'atom' (which means 'not cleavable' in Greek). He held that matter consisted of atoms and that the atoms themselves were indivisible. But Aristotle who spoke of only four basic elements in the universe opposed him. Aristotle's ideas held sway until the European Renaissance, which initiated a revival of ancient learning. This paved the way for the scientific exploration of matter and the industrial revolution. Experiments rather than philosophical musings marked a remarkable phase of discovery and invention of new materials from the second half of the 17th century (Box 1).

Box 1

Understanding Matter—An Historical Overview

One of the early pioneers who extended the human vision of the material world is Robert Hooke (1635–1703) of England. His microscope magnified materials 50–100 times.

Robert Boyle (1627–1691) put forward the idea that the world consisted of only a limited number of elements. Joseph Priestley (1733–1804), Cavendish (1731–1810) and Lavoisier (1743–1794) discovered oxygen, hydrogen and nitrogen, respectively.

On a practical level, Rene de Reaumur (1772) sketched the structure of hardened steel. With a rare insight, he held that a single grain of steel would reveal a set of molecules and voids. Charles Goodyear accidentally discovered vulcanisation in 1839, after about five years of experiments. Until then the hardening effect of sulphur on rubber was unknown.

Henry Bessemer patented in 1856 his process of steel-making on a large scale. Henry Sorby (1860) used a light microscope to study the microstructures of rocks and metals. Alexander Parkes, a Birmingham chemist, invented the first genuine plastic in 1862. Celluloid was commercialised in 1869. And the entirely synthetic plastic was invented only in 1909.

In 1808, John Dalton held that every element had its own unique kind of atom. An Italian physicist, Amedeo Avogadro

disclosed (1811) the composition of water as two atoms of hydrogen and one atom of oxygen. He also coined the word, molecule, meaning a combination of two or more atoms.

Another early landmark was the publication of what came to be known as the *Periodic Table of Chemical Elements* brought out by Dmitri Mendeleev and Julius Lothar Meyer (1870). Interest in chemistry led to the development of a process to produce aluminium metal from its ore by 1886.

In Germany, Wilhelm Roentgen (1845–1923) discovered X-rays. Sir William Bragg (1862–1942) used X-rays to determine the structure of crystals. His son Sir Lawrence Bragg (1890–1971) pioneered X-ray crystallography—an important technique for studying material structure. The younger Lawrence was only 25, when he and his father received the Nobel Prize in 1915!

The next significant phase of discovery related to electricity. Michael Faraday (1791-1867), Benjamin Franklin (1706–1790) and Alessandro Volta (1745–1827) discovered various aspects of electricity.

When electricity was used to study matter, it resulted in the discovery of the electron in 1897. Joseph Thomson (1856–1940) showed the electrons were much lighter than hydrogen. He held that all atoms have one or more electrons.

In France, Henry Becquerel (1852–1909) found that a certain metal showed some properties like X-rays. It turned out to be uranium. Actually, it was a re-discovery as the metal was discovered almost a century earlier in 1789 by a German chemist, Klaproth.

Pierre and Marie Curie (1867–1934) purified pitchblende and produced a few crystals that yielded powerful rays. Marie called it polonium. Later, the Curies found radium and named the phenomenon of the rays, radioactivity. They were awarded Nobel Prize for their discovery.

Research on radioactivity in Cambridge (UK) continued under Ernest Rutherford (1871-1937). He established the electrical structure of matter and the nuclear model of the atom. In 1919, he split the atom by natural means.

Rutherford and his student, Frederick Soddy (1877–1956) unravelled the atomic structure step by step. His colleague

Niels Bohr (1885–1962) played a key role in describing the nature of the nucleus of the atom. He proposed that the electrons change their energy by 'jumping' between stationary states. Another student of Rutherford, James Chadwick (1891-1974) discovered the neutron in 1932.

Frederick Soddy suggested (in 1913) that atoms of the same element with the same chemical properties can have different atomic weights.

Albert Einstein (1879–1956) held that matter and energy are different forms of the same thing. His famous equation ($E = mC^2$) showed how to calculate the tremendous energy that can be had from conversion of a small quantity of matter.

An Italian-born physicist, Enrico Fermi (1901-1954) bombarded uranium with neutron, splitting the atom in the process without realising it. In 1932, John Cockcroft and E.T.S. Walton split lithium with protons. Soon German scientists split uranium bombarding it with neutrons. Ten years later, Fermi and his colleagues lit the world's first atomic fire in 1942. And the first nuclear explosion was conducted in the New Mexican desert in 1945.

In 1906, Max Planck suggested that the energy of a system must jump from one value to another in discrete steps or quanta instead of changing continuously. He explained that black body radiation was quantified, that is, light emitted by hot bodies which turns from red to yellow and blue as the temperature is raised.

A Dutch physicist, Heike Kamerlingh Onnes discovered superconductivity, which transmits current without resistance. In 1911, he found that mercury lost all resistance to electric current when cooled by liquid helium to within a few degrees (4.2) of absolute zero. The phenomenon puzzled scientists for more than 40 years.

Einstein had proposed that light too should be considered in terms of discrete packets of energy behaving like particles (later called photons). Interestingly, Einstein found that the size of a single molecule of sugar was about one nanometer in diameter. His understanding of matter at the atomic level reflected the views of India's famous scientist, Satyendra Nath Bose, in the 1920s.

It is now known that nanoparticles can be found in Ming dynasty pottery in China and stained glass windows in medieval churches though the craftsmen had no idea of nanoparticles.

In recent decades, a few outstanding scientists have advanced the understanding of matter *at the atomic level*. Indian scientist Satyendra Nath Bose (1894–1974) proposed in 1924, a new way of explaining radiation (Box 2). It resulted in the discovery of a new form of matter. Bose described light as if it were a gas of massless particles (called 'photons') that do not obey the classical laws. Einstein applied the reasoning of Bose to a real gas and obtained a new 'formula' called Bose-Einstein distribution. It was predicted that extremely cold atoms should condense into a single quantum state, later known as Bose-Einstein condensate. Such a condensate could not be created until scientists developed lasers and mastered the technique of manipulating

Box 2

S.N. Bose and the Mystery of Matter

An Indian scientist's insight resulted in the discovery of a new form of matter and has given a new insight into the mystery of matter. Up until the early 1920s, scientists imagined the electromagnetic radiation as a continuous stream. A new idea that the radiation comes in discrete energy states gained currency in the mid-1920s, following a new state of matter predicted by Satyendra Nath Bose.

At the age of 22, Bose translated a German text of Albert Einstein on General Relativity into English. Einstein was delighted and arranged for permission to use the translation in India. Bose later sent his article on Planck's radiation law, proposing a totally new way of explaining it. Einstein was so impressed that he himself translated it into German and arranged for its publication. The two scientists met in Berlin in 1925. Bose returned to Dacca and later moved over to Calcutta.

Bose treated light as a gas of massless particles that come in small discrete packages (now called photons) that obeyed a new kind of statistics. Essentially, he assumed that the waves and particles of light are the same. Einstein applied Bose's reasoning to a gas of massive particles and developed a new theory to indicate how energy is shared by particles in a gas and predicted parallel behaviour of light and atoms. Later all those particles that obeyed Bose-Einstein statistics were named 'Bosons'.

Both the physicists jointly predicted a novel state of matter, which is now known as Bose-Einstein condensate. They said it would form when atoms suddenly condense into a single wave of matter, lose their identity, and cool down to absolute zero (–273.15°C). The atoms would settle into a single quantum state. Known as the super atom, the cloud would be neither liquid nor solid. It is in line with quantum mechanics, which holds that waves and particles are the same!

In the early 1920s, there was no way of producing near absolute zero temperatures and to verify the prediction of Einstein about the strange behaviour of atoms under extremely low temperatures. It was only in 1995 that the theory could be confirmed. At a conference in Capri, Italy on laser spectroscopy, a scientist, Eric Cornell, reported the results of an experiment conducted with Carl Wiemann of the University of Colorado. The two scientists had cooled a few thousand rubidium-87 atoms to just 200 billionth of a degree above absolute zero and made the world's first Bose-Einstein condensate. Wiemann explained that the condensate was a new form of matter and behaved completely different from any other material. Besides rubidium, five other elements, viz., lithium, sodium, hydrogen, helium and potassium had been individually used to form Bose-Einstein condensate. Cesium was the seventh element to be so used. The two scientists and a German, Wolfgang Ketterle (of MIT), were awarded the Nobel Prize in 2001 for the experiments.

The technique does not merely indicate intellectual curiosity. The idea has been useful in producing the first atom laser, which has wide applications including precision gyroscopes, atomic clocks and microchips.

individual atoms and keep them trapped. The first Bose-Einstein condensate was created 65 years later!

The Casimir Force

The traditional idea about vacuum as being just 'nothing' was given up, after scientists realised that the electromagnetic waves in a vacuum could not be completely eliminated. Hendrik Casimir, a Dutch physicist (1909–2000), first predicted the force in 1948. Modern physics assumes that a vacuum is never completely empty but has some energy as well. The difference in the energy between two mirrors or plates in a vacuum, for instance, accounts for the force that attracts the plates (Fig. 3.1).

It was difficult to measure the force with the equipment of Casimir's time. Today, it is possible to measure such a tiny force with better accuracy. The effect too has become relevant as nanoscale structure devices and systems are being developed, where measurement of tiny forces is crucial

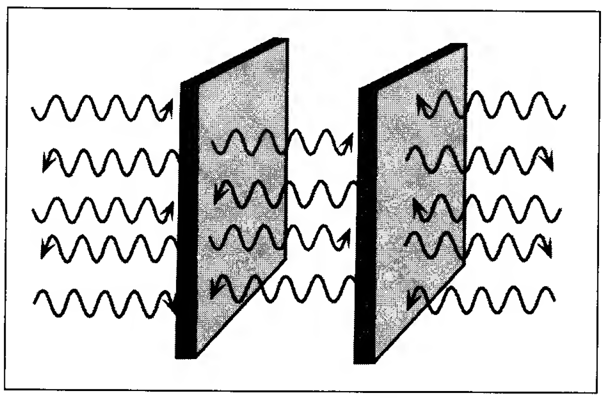


Fig. 3.1: A Force from Nothing! When two mirrors face each other in a vacuum, fluctuations in the vacuum exert radiation pressure on them, attracted by a force, called after its discoverer, Casimir. It affects the working of nano-electro-mechanical systems. It can also be a repulsive force with the right choice of electrical and magnetic features in devices for identification.

(e.g., car air bags that pop out in front of the driver in case of a collision).

It has been found that the Casimir force can be substantial, when the distance between two neutral objects is of the order of 10 nm. Scientists wonder whether Newton's inverse square law of gravity would still hold good even at a very short distance. The Casimir force, though relevant to nanoscience, is still a mystery.

Richard Feynman: An Unconventional Guru

The invention of the transistor (1947) and the integrated circuit (1958) led to smaller and smaller components for electronic devices. A year after the first integrated circuit was built, a brilliant physics professor in the US and a Nobel laureate, Richard Feynman (1948–1988) described how physics and machines would be different at the microscale. In an original analysis, Feynman predicted that new kinds of forces and effects would have to be encountered at the atomic level and that quite different problems would arise in the manufacture and reproduction of new materials. He urged people to think at the scale of the atom itself.

The New York Times called him "the most brilliant, iconoclastic and influential of the post-war generation of theoretical physicists". At the age of 13, he went to the library to borrow a book on calculus and had to tell a curious librarian that the book was meant for his father! He grew up to be an unconventional genius, who endeared himself to his students by his brilliance and wit.

In his famous presentation to the American Physical Society at Caltech on 31 December 1959, 'There's Plenty of Room at the Bottom', Feynman pointed out that the principles of physics did not speak against the possibility of manoeuvring things by atom. He indicated that it should be possible to write all of the 24 volumes of the *Encyclopaedia Britannica* on a pinhead without violating any laws of

physics. The talk was given a year after Jack Kilby, an American electronics engineer, demonstrated the first integrated circuit ever made from a simple piece of semiconductor. Feynman was quick to realise that it would be possible to make them smaller and smaller until Nature limits their size. He predicted that once the language of atoms was decoded, it would be possible to precisely place one atom against another.

Feynman offered a prize of $1000 to anyone who proves his prediction about fitting the *Encyclopaedia* on a pinhead. The challenge was to write a page 1/25000th its normal size. It was achieved only in 1985. Feynman's offer of another prize for the creation of an atomic structure was quickly claimed.

Before molecular biology was recognised as a special study, Feynman even spoke of a molecular 'doctor' who would 'read the health of a cell'. He described why one would want to use micro machines, how one could build them and how the physics underlying them would be different from the traditional machines.

His dream of progress in the nanomechanical area has been realised. Nano devices could be inserted into our bodies for imaging, diagnosis and drug delivery. It is also possible to write electronically the entire encyclopaedia on a pinhead. The power to write small and read it quick has increased to an amazing degree that computer engineers envisage that it would be possible to store not one encyclopaedia but all the books in the world on a surface no longer than a credit card! Feynman's vision of storing and retrieving information has come true in the form of the Internet, one of the finest of human achievements, though Feynman could not have possibly foreseen it.

Feynman's talk did not trigger any new initiative immediately. However, it prepared scientists to accept the future shock set off by advances in molecular biology,

synthetic chemistry and computer science. In fact, many of his dreams have been fulfilled in recent times. Following the use of scanning tunnelling microscopy, researchers have been able to see single atoms and manipulate them at will.

In the early 1970s, researchers developed a process to deposit a thin layer of high-purity semiconductors on a surface. Work proceeded in the mid-1970s to develop molecular electronic devices. Computer engineers developed systems based on single molecules designed for logic switching and signal propagation.

In 1974, the word 'nanotechnology' was introduced by Prof. Nori Taniguchi of Japan, while handling machines, which had tolerances in terms of a micrometre. The same year, the first such device was patented by IBM scientists (Aviram and Seidon).

Mr Nano

Several conferences discussed the topic. Prompted by these developments, a young student of MIT (US), Eric Drexler, published the first technical paper on 'Molecular Nanotechnology' (1981). The subject was new and Drexler had described something unconventional.

A year later, Binnig and Rohrer described their new invention, the scanning tunnelling microscope (STM) in 1982. For the first time, individual atoms could easily be imaged. It was hoped that by attaching certain tools to the tip of an STM, really small structures could even be built. This must have prompted Drexler to propose something even more daring. In 1983, he presented the most complete description of a molecular computer at the Second International Symposium on Molecular Electronic Devices. He also published the first book on molecular nanotechnology *Engines of Creation* in 1986. He held that molecular machines could be made imitating biological models and that complex structures could be built based on chemical reactions.

His ardent advocacy of nanotechnology earned him the nickname, 'Mr Nano'. The Foresight Institute he had founded serves as a forum for in-depth consideration of ideas related to nanotechnology and its promotion.

Discovery of Buckyball

At about this time scientists announced a discovery, which would enable them to realise some of Drexler's ideas. In 1985, Richard Smalley and Robert Curl, chemists at Rice University in Texas along with astronomer Sir Harry Kroto of the University of Sussex (UK) discovered a new form of carbon. They were studying the structure of carbon molecules on red giant stars. Assisted by graduate students, James Heath and Sean O'Brien, they created the star-like conditions by bombarding carbon with lasers. The scientists found a large proportion of very stable clusters with 60 carbon atoms each. They constructed a model of the cluster as a molecule with 20 hexagons and 12 pentagons. It was called carbon-60, a soccer-ball shaped molecule made of 60 carbon atoms joined together as hexagons and pentagons. They named the molecule buckminster fullerene, because its structure resembled the geodesic dome invented by Richard Buckminster Fuller. It was soon known as buckyball. The new form of carbon (3-D nanoscale carbon 'cages') could stand very high amounts of heat and pressure. It intrigued many scientists and triggered widespread interest in carbon-based molecular structures. The three scientists won the Nobel Prize in 1996 for their discovery (Fig. 3.2).

In 1988, three chemists at AT&T's Bell Labs in New Jersey (Paul Alivisatos, Mounji Bawendi and Michael Steigerwald) showed that gold emitted light differently at the atomic level. Many observers regard this finding as a major turning point in the development of nanotechnology. For the first time the behaviour of atoms was seen differently from the prediction of classical theory. It demonstrated

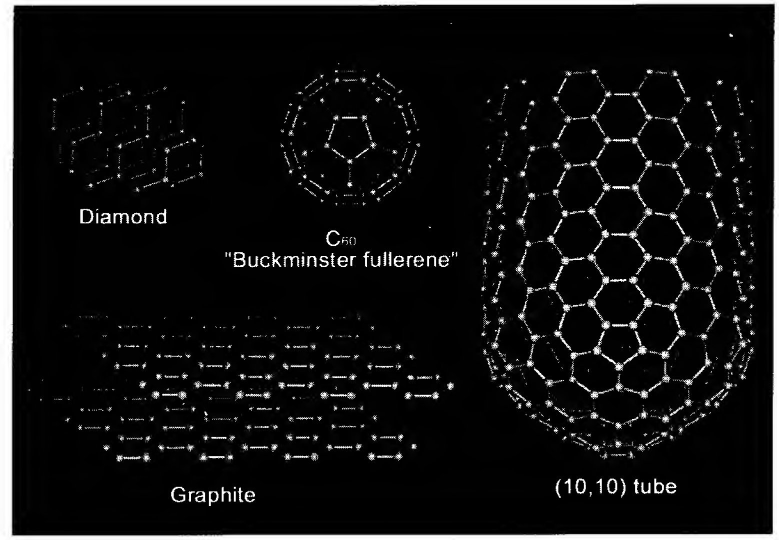


Fig. 3.2: Models of different forms of carbons (not to scale). If the forms were actually the size shown, the nanotube would extend more than a kilometre!

quantum mechanics, the physics that explains why very small things behave differently from their bigger selves.

By the end of the 1980s, Ahmed Zewail, a brilliant chemist working in the US showed that movement of atoms in molecules could be seen with femtosecond timing. A femtosecond is millionth of a billionth of a second or a quadrillionth of a second. It is one second divided by ten raised to the power of 15. It enabled scientists to witness the chemical events that occurred in a quadrillionth of a second. The split-second world of the femtosecond is now visible. His use of the laser to see atoms was likened to Galileo's use of the telescope. Zewail tried his femtosecond laser on literally everything that moved in the world of molecules. He was awarded the Nobel Prize in 1999.

The basic understanding of the nature of liquids and glasses at the atomic and molecular levels has advanced

further. Liquids and glass have no structure and are called amorphous. However, it has been pointed out that the atoms and molecules in a liquid are quite 'organised'! In 2002, a chemist at the North Carolina State University in the United States, James D. Martin, and his team discovered the chemical principles that would enable scientists to design the compositions and structures of several glasses and liquids. Electrons moving within an atom have been tracked in a unique experiment (2002) at the Vienna Institute of Technology. The shortest laser pulses ever generated were used for the purpose. The pulse seemed to travel faster than even the vibration of atoms. New views of matter may well come up. Scientists hope that new optical and electronic properties could be inserted into materials.

The 1980s saw the advent of what is known as laser cooling, which opened a new chapter in ultra-low temperature physics. Samples of dilute atom clouds in the micro kelvin range were created and used for precision measurement. Nano kelvin temperatures are needed to explore gases such as the Bose-Einstein condensates.

Reality of Matter: A Mystery

Einstein said that matter is nothing but energy. But energy is beyond our physical perception. As a German science journalist, Falk Fisher puts it, "A rose is a rose is a rose. But at the level of individual atoms, this certainty becomes shaky. Whenever physicists refer to individual atoms, they are actually referring to nothing more than clicks in detectors. No physicist can say whether a particle exists continuously on its path from the source to the detector. A particle is a particle only if it results in a click. If there is no click, its very existence is in doubt!"

When atoms near absolute temperature, they cannot make any 'impact' and so cannot be seen as reality. The

moment they absorb a single photon, Bose-Einstein condensate vanishes from our eyes. It does not, however, mean the condensate does not exist. It exists in a different world, which obeys a different law and logic other than the one where a cause is followed by effect as we experience a phenomenon in our daily life. Perhaps a quantum computer will one day function in such a world.

Bose-Einstein condensate is thus envisaged as matter in virgin form, before it takes on some 'information' so as to be visible to us. It is a deeper reality, a behind-the-stage phenomenon hidden from us. It only shows that what we call matter is still a mystery, worthy of our deep reflection. We cannot simply say, "It does not matter!"

4

NANOMATERIALS: WONDERS UNLIMITED

It is amazing what one can do by just putting atoms where you want them.

—Richard Smalley (Nobel laureate and co-discoverer of the buckyball)

Carbon is the only element in nature found with varying physical and chemical characteristics. Until the discovery of the buckyball in 1985, carbon was known only in two forms: graphite and diamond. The new form of carbon kindled the curiosity of scientists in Germany and the US who made buckyballs in large quantities and studied them in detail.

In 1991, a Japanese electron microscopist, Sumio Iijima, discovered in his microscope at Tsukuba, Japan, something strange in a new form of pure carbon with a few nanoscopic threads. He found closed graphite structures including nanoparticles and what became known as nanotubes. It is actually a stretched out form of a buckyball, a sheet of carbon curved into a cylinder capped at each end (Fig. 4.1).

The material was found to be stronger than conventional carbon. Shortly afterwards, Thomas Ebbesen and Pulickel Ajayan from Iijima's laboratory produced nanotubes using graphite rods and electricity. Some of the hot plasma resulting from the vapourised carbon recondensed as carbon nanotubes. Different carbon modifications (tubes within tubes, later called multi-walled carbon nanotubes) were made subsequently (Fig. 4.2). Every rolled-up graphite-like sheet contained millions of atoms arranged in a hexagonal array. The discovery sparked off research in several countries.

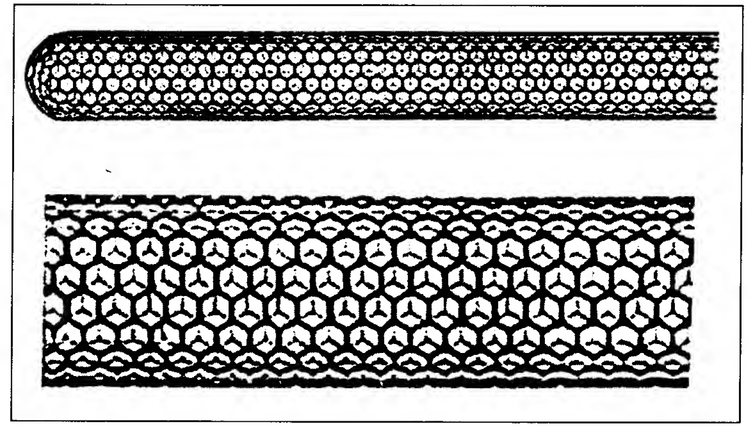


Fig. 4.1: Carbon nanotube (top) with its detailed structure magnified.

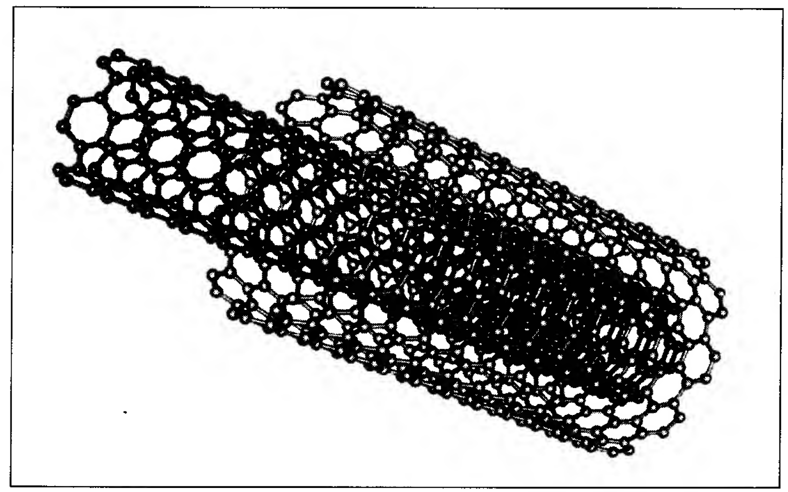


Fig. 4.2: A double-walled (two-layered) carbon nanotube, useful for making composite materials with added strength. They are relatively easier to make than the single-walled nanotubes.

Two years later, in 1993, Iijima and IBM independently developed single-walled nanotubes that were graphite layers seamlessly wrapped as cylinders. Iijima developed the chemical vapour deposition (CVD) technique for producing individual shells of the new material. The technique uses a carbon-bearing gas such as methane and as it decomposes, carbon atoms emerge to be recombined as nanotubes. CVD is a catalytic process in which metal nanoparticles react with a hydrocarbon gas to produce highly pure nanotubes. In yet another method, graphite rods were subjected to laser beams. In this and another method (known as arc discharge) 30–70 per cent of the output would be carbon nanotubes, while the rest would be amorphous carbon. Multi-walled nanotubes need a mixture of hydrogen and acetylene as the source gases, while a single-walled tube—a single layer of carbon atoms—requires hydrogen and methane.

An IBM scientist, Don Bethune, is reported to have done research independently on carbon nanotubes. Interestingly an American chemist, Howard Tennent had filed a patent for a carbon nanotube, then called 'fibril' measured in angstroms (tenths of a nanometre). Though fibrils were produced in bulk, the name 'carbon nanotube' prevailed. When the IBM team demonstrated that it could not only 'see' individual atoms but could also manipulate them efficiently, it was considered possible to realise one of Feynman's dreams. At that scale, it would be possible to write the entire *Encyclopaedia Brittanica* on a pinhead! This ability to manipulate atoms and molecules triggered further research on the behaviour of matter at the atomic level.

Following Iijima's discovery, scientists in the United States and several other countries stepped up their investigations into the properties of carbon nanotubes, which were theoretically predicted. They included high strength with low weight, stiffness, low density, regular structure, good heat conductance and strange electronic properties. Much

has been learnt, though a lot remains to be understood. Interestingly, simulations in supercomputers have been made leading to realistic predictions and verification in actual experiments.

The unique electronic and mechanical properties of carbon nanotubes have motivated researchers to explore their potential in a wide range of applications: nanoelectronics, sensors, displays, batteries and nanoscale electrodes and high-strength composites. Carbon nanotubes and other nanomaterials continue to reveal surprising features of materials at the nanoscale and open up a new world of wonders seemingly unlimited.

In the US, Rice University in Texas was among the institutions quick to grasp the significance of the new development. The first laboratory in the US dedicated to molecular nanotechnology research was established headed by Prof. Richard Smalley, Nobel laureate. It was followed by the establishment of a molecular robotics laboratory at the University of Southern California in 1994.

The world's tiniest carbon nanotube that has been produced is 0.4 nm wide. Experts say that this is the theoretical limit. The tube has been produced by NEC Japan and the Hong Kong University of Science and Technology.

Indian scientists started research on carbon nanotubes in the early 1990s. China too has emerged as one of the leading countries in the study and application of nanoscience. It has produced a carbon nanotube and continues research on various aspects of nanotechnology. The country ranks third after the US and Japan in the publication of technical papers on nanotechnology.

One Hundred Times Stronger than Steel

A single-walled carbon nanotube is unusually strong and stiff. It is one hundred times stronger than steel. Its strength-to-weight ratio is 600 times that of ordinary steel. A typical

nanotube is at least 1,000 times longer than it is wide. This feature is technically known as large length-to-width ratio or a high aspect ratio. This quality adds to the tube's reinforcement, as it resists the movement of any molecule and makes the nanotubes good electron emitters. In vacuum it can withstand 1,000ºC. Incidentally, a strange behaviour on the part of the single-walled nanotube was noted: it spontaneously exploded when exposed to an ordinary camera flash! Moreover, carbon nanotubes are sticky and clump together. A novel way of separating them has been recently suggested by mixing them with single-stranded DNA. It is reported that the DNA sticks to the tubes, making it easier to separate them.

Carbon nanotubes are exceptionally strong against any crack or damage. They are therefore exploited in making the next generation of light but strong composite materials. As the nanotubes are hollow, tubular and caged molecules, they are ideal for gas or lithium storage and for drug delivery.

An important feature of the carbon nanotube was demonstrated in 1997. That is electrical conductivity of the tube. A carbon nanotube has enormous capacity to conduct electricity and transports heat better than diamond. However, the minuscule cylinders roll up in different directions resulting in different electronic properties. It has not been easy to control the diameter as well as crystal structure of the tubes. An improved variation of the CVD process has beeen found to ensure uniformity, a consistent production of highly conductive nanotubes.

The nanotube's ability to conduct electricity depends on the precise arrangement of its carbon atoms. Accordingly, the nanotubes, which are rolled sheets of graphite, exhibit a range of electronic properties, functioning as a conductor or semiconductor or a combination of the two forms. A team of Harvard scientists has recently found that the outcome

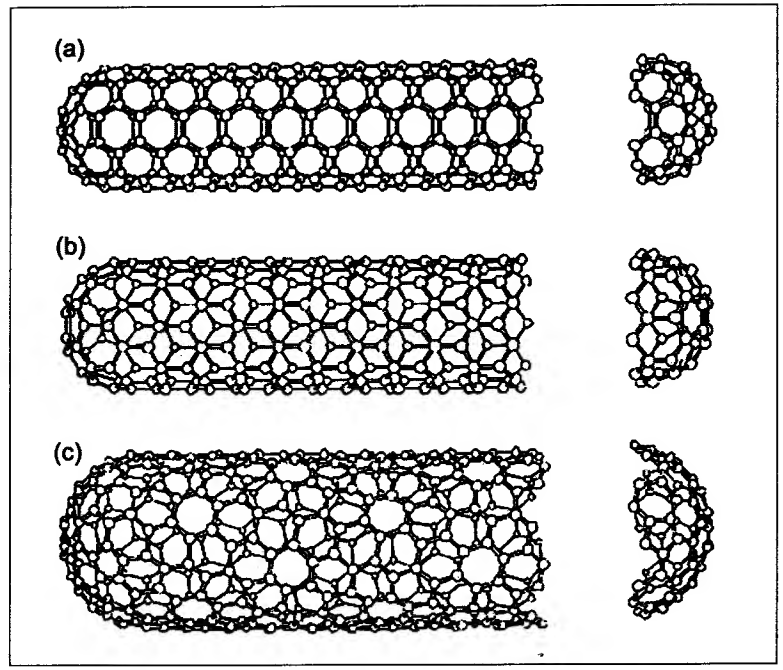


Fig. 4.3: Different arrangements of carbon atoms in a nanotube. (a) 'armchair' configuration; (b) zigzag formation and (c) helical pattern. (The gaps in the tubes are shown to indicate that the actual length of the nanotube would be different.)

depends on whether the sheet is made from one or many layers as well as the angle at which the sheets are rolled. A zig-zag pattern of the tube has been found not fully metallic, while an arm-chair pattern is fully metallic with no energy gaps (Fig. 4.3). German scientists have reported a new way of separating the metallic nanotubes from the semiconducting ones.

Two Approaches: Top-down and Bottom-up

Basically there are two ways of making nanoscale objects: top-down and bottom-up approaches. The top-down approach refers to the building of nanostructures of

progressively smaller and smaller dimensions using larger parts. The bottom-up approach calls for assembly of nanostructures (e.g. nanowires) from atoms and molecules. Self-assembly of nanotubes has been found to be a useful feature.

Self-assembly—A Useful Feature

Scientists have exploited the ability of biological molecules to self-assemble in their efforts to provide nanoscale materials. Self-assembly, as it is well known to biologists, is simply a process where biological molecules in the right mix would form unique structures (e.g. cells and organs). Scientists found that nanotubes could be used as a self-assembling frame on which objects such as chemicals and molecules could be mounted.

The National Academy of Sciences, USA has published details of the research in the field done by Purdue University. The technique would enable scientists to custom-build nanotubes for molecular electronics and biomedical devices. Researchers at the University of Massachusetts, Amherst, have developed innovative techniques to promote the self-assembly of nanoparticles. One method envisages creation of three-dimensional capsules from nanometer-sized particles. The researchers have found that the particles, suspended in oil, will self-assemble around a drop of water. Yet another method turns the oil-soluble nanoparticles water-soluble, simply by shining light on them and adds new features like luminescence. These techniques would be useful in several applications such as medical imaging and diagnostics, as well as development of drug delivery.

The self-assembly process has several applications. Nanoscale (or minuscule) objects are assembled at specific sites on another substrate for detection and diagnosis of disease, as well as fabrication of novel electronic systems. For instance, proteins and DNA can be attached to carbon

nanotubes for further processing, resulting in the synthesis of new materials. Though chemical self-assembly allows fabrication of a large number of devices in a cost-effective manner, there are engineering problems in practice.

An interesting experiment is noteworthy. Self-assembly techniques can be used to produce organic (instead of carbon) nanotubes. A team of scientists of Purdue University has produced a helix, based on guanine and cytosine bases that self-assemble through hydrogen bonds. A remarkable feature of this technique is the capacity to modify the nanotube's properties by adding conductive polymers or photoactive elements. It means that the nanotubes can be used to make new materials, and electronic devices including molecular-scale circuits.

In order to ensure a high level of reliability, one of the approaches being tried is a defect-tolerant architecture. The approach is different from today's technology of building microelectronics as perfectly as possible. Nanoscale systems may be designed to work even with faulty parts. For instance, atomic scale switches can function in a defect-compatible structure.

As of today, nanotechnology is mostly at the top-down stage: the nanostructures are made by machining and etching techniques rather than the bottom-up way of building organic and inorganic structures atom by atom. The bottom-up technique is used for example, in making ultra-thin films that are synthesised wih thousands of material layers. Scientists have however started exploiting the ability of biological molecules to self-assemble and have produced nanoscale materials. Scientists at the University of Chicago have engineered proteins that would form the core for gold wires 80 nm wide. Protein fibres coated with silver and gold could be useful nanowires in electronics.

Tests and Challenges

Nanotubes no doubt serve as reinforcing fibres in composite materials. Nanotubes can be made from silicon, gallium arsenide and cadmium selenide. They can be given the positive features of semi-conducting nanowires. However, several materials have yet to be tested. Aluminium, for example, behaves in a strange manner at the nanoscale level. Scientists have yet to fully understand how aluminium would function at the most basic level, when a one-atom thick layer of aluminium slides over another. In aluminium, which is three times lighter than copper, atoms bond in a manner different from copper. Aluminium is 32 per cent stronger than copper. Under simulated conditions, aluminium scores over copper in many ways and behaves like ceramic that may be of use in computer circuits.

Scientists have been able to conduct experiments on a nanoscale particle, while carrying out simulations atom by atom on a similarly sized particle in a supercomputer. This has enabled researchers to make hardness measurements on individual silicon nanospheres. These particles are reported to be four times harder than silicon itself. The hardness varies between that of sapphire and diamond. The research is aimed at finding out similar materials with enhanced properties.

Size Fascinates

The size of nanomaterials is a fascinating feature. For example, the electronic structure of metal and semiconductor nanocrystals differs from their bulk form or their isolated atoms. Size affects the structure of nanoparticles of several materials. Their melting point and the electronic absorption spectra become different. Size-determined effects include thermodynamic, electronic, spectroscopic, electromagnetic and chemical properties.

Materials research often springs up surprises. Nanoscale molecules with characteristic diamond structure have been isolated from petroleum. Called *diamondoids*, these hydrocarbon molecules, 1–2 nm in size, are isolated from natural gas condensates. These are fundamentally new materials that may well have use in drug delivery.

Another area of growing interest is in evolving new materials such as conductive plastics or even steel-like plastics. They can be created by a mixture of carbon nanotubes with other materials. Nanotubes without carbonaceous particles can be made to have precisely defined properties. The challenge lies in producing materials according to well-defined configurations instead of accepting random results.

Nanoparticles show unusual properties. For example, gold is inert in its bulk form, but if the diameter of the particle is reduced to a few nanometres, it catalyses carbon monoxide into carbon dioxide. Similarly, titanium dioxide particles in sunscreens, when reduced in size, would absorb the ultraviolet radiation without causing the side effect of whitening on the skin.

It has been recently demonstrated that the average size and shape of a nanoparticle can be watched during its growth in real time.

Spit and Spot!

One of the problems identified in making nanotubes made of carbon was its insolubility in water. This shortcoming had come in the way of utilising the tubes in several medical applications. A team of scientists in Italy discovered that attaching organic elements to nanotubes would make them soluble. A group of scientists in Los Angeles found that if they encircle nanotubes with starch molecules, the tubes will be dissolved in 'aqueous solution'. Besides starch, gum Arabic and glucosamine were also found to dissolve nanotubes in water. The scientists in fact found that when they spat

into the aqueous solution of starch-wrapped nanotubes, α-amylase in saliva would destabilise the solution and make the nanotubes solid!

Mass production of nanotubes of uniform nature is a challenge. Still each day 2.5 tonnes of carbon nanotubes are produced in the world (2003). The demand is expected to go up. Nanotechnology is bound to bring about a major change in materials, just as plastics had impacted on business. Understanding a material's defects at the quantum level has become essential, since nanotechnology involves thin layers of material, which would be under considerable strain, while responding to repeated sensing of electrical current. Chemical bonding between nanotubes and polymers is another area of interest. Supercomputers are being used to better understand the properties of carbon nanotubes. Several breakthroughs in large-scale production of carbon nanotubes are awaited. In a unique experiment, it has been found that large-scale, ordered patterns of nano-wires could be assembled, when they are floated on a water surface, guided by computers. The practice is similar to the practice of transport of timber logs floated down rivers.

Nanotubes can be made from silicon, gallium arsenide and cadmium selenide. They have all the positive features of semiconductor nanowires and carbon nanotubes. Even as new materials are explored at the nanoscale level, it has been realised that better control is needed in organising their production. Well-defined configuration is required to get integrated systems. It is called directed assembly of structures, using chemical vapour deposition, which involves processing materials through a gas stream. This is widely used to direct the assembly of carbon nanotubes in a variety of pre-set orientations. In 2002, a joint US-Chinese team of scientists in Beijing found a way of synthesising single-walled nanotubes that are 20 cm long with a width of

0.3–0.5 nm, using the chemical vapour deposition process.

Researchers at the Meijo University (Japan) have reported success in growing single-walled and multi-walled carbon nanotubes in a novel way, using camphor, a green plant product. This is in sharp contrast with the conventional process based on petrohydrocarbons such as methane and benzene. In India, scientists at the IIT, Mumbai, have synthesised CNT from turpentine and other plant-based oils such as those from linseed, mustard and cotton seed. Some of these CNTs, it is reported, can store appreciable quantity of hydrogen. The plant oil-based synthesis may be more economical than the petroleum-based precursors used for making CNTs.

Though the capability of a nanotube is experimentally proved, there are numerous problems in handling large amounts of any given type of material. The metallic portion in a mixture of carbon nanotube has to be manually eliminated to recover the semiconducting areas—a process unsuitable for mass production.

An Array of Nanomaterials

Nanomaterials include many materials other than nanotubes: nanoparticles, nanowires, nanoporous solids and nanocapsules and DNA chips. Chemists have synthesised molecular structures at the nanoscale for making them functional in several applications (Box 3).

Several methods of synthesising and assembling nanoparticles, and nanowires of several inorganic materials have been discovered. Nano-structured polymers have also been obtained through the process of self-assembly.

Charles Lieber's group in the US has made nanowires (several micrometers long and about 20 nm wide) from various materials such as silicon, indium phosphide and gallium nitride. It was reported that they found nanowires that are ten times thicker than single-walled nanotubes and

are more suitable than nanotubes for mass production and integration with nanoscale devices.

Nanowires cannot, however, be made by pulling a piece of metal! They are constructed bottom-up from materials such as silicon using catalysts such as gold nanoclusters. A variety of electronic devices have been made, using bottom-up manufacturing techniques. Some transistors and diodes have been built by growing nanowires from different semiconductors. An interesting finding is that the properties of semiconductors are controlled by dopants

Box 3

Examples of Nanomaterials

	Size	***Materials***
Nanocrystals	dia 1–10 nm	Metals, semiconductors, magnetic materials
Clusters (quantum dots)	dia 1–100 nm	Ceramic oxides
Nanowires	dia 1– 100 nm	Metals, semiconductors, oxides, sulfides, nitrides
Nanotubes	dia 1–100 nm	Carbon, layered metal chalcogenides
Nanoporous solids	Pore dia 0.5–10 nm	Zeolites, phosphates, etc.
Two-dimensional arrays of nano-particles	Several nm″ – µm″	Metals, semiconductors and magnetic materials
Surface and thin films	Thickness 1–1000nm	A variety of materials
Three-dimensional structures (superlattices)	Several nm in three dimensions	Metals, semiconductors, magnetic materials

(boron, for example). In one experiment, two different nanowires—one made of gallium nitrade and the other of silicon – were used to create a transistor. Several such transistors could constitute the nanowire for memory. Nanowires could be coated with charged molecules too. The advantage is the enormous reduction in power demands.

Using nanowires of silicon and germanium, researchers at Harvard University grew multiple shells. Lieber and his team demonstrated a field-effect transistor based on a nanowire. A remarkable feature of this feat is that it has proved the idea of a functional nanostructure. It would mean that the desired functions could be built into the nanowires even as the latter are being synthesised.

Nanosprings, like coil telephone cords, have been made recently. Nanosprings can be used in composites, nanosized magnetic field producers and detectors. Researchers used electron microscopes to evaluate the helical silica spring in heated conditions. They used an atomic force microscope to bend the spring. The mechanical energy and the flexibility of the spring are found acceptable.

An advantage of nanocrystalline materials is that they combine high strength as well as ductility (capable of being drawn into a wire). This is remarkable, because generally these two qualities—strength and ductility—do not coexist! The possibility of having both the qualities was proved recently by scientists who created a copper nanostructure. It was made by using the copper at a low temperature and then raising its temperature by nearly six times.

As carbon nanotubes and nanofibres self-assemble, researchers have used them in a novel manner. Vertically aligned carbon nanofibres have been used as templates to make nanopipes. The process involves a series of delicate steps starting with the deposit of nickel particles as catalyst sites for the growth of nanotubes. The resulting nanopipes,

Box 4

Nano Crystals and Scrolls

Nano crystals are recovered from common scrap that would normally be melted down for reuse. Nano crystals (typically 10 nm in diameter) are larger than molecules but smaller than bulk solids. As the crystal grows in size, its properties can vary significantly as it has virtually all surface and no interior. They are often harder and stronger (by 200 to 300 per cent) than the bulk form. Added to plastics and other metals, nano crystals are useful in making stronger but lighter car bumpers and airplane parts, besides new types of sensors and computer components.

A single-crystal nanotube has been developed. Unlike carbon nanotubes, which are either semiconducting or metallic, gallium nitrade nanotubes have been found to be only semiconducting. What is more, their optical properties are remarkable. As they readily emit ultraviolet and blue wavelengths of light, the single-crystal tubes have applications in opto-electronic devices as well as chemical and biological sensors. Moreover, nano crystals are reported to have overcome their 'fear' of water and so they can be used to image even living embryonic cells.

It has been found that some nanoparticles synthesised in the laboratory (2001) appear to absorb light as dust particles do in interstellar space. Called carbon onions (multi-layered balls) the particles have practical applications in energy storage and fuel cells.

Another alternative to nanotubes are carbon nano scrolls, which are also pure carbon but with some differences. While nanotubes are carbon sheets in a tubular form capped at each end, nano scrolls are curled up sheets (averaging 40 layers) without end caps. The latter has additional surface area. Nanotubes are made at high temperatures, whereas nano scrolls can be created at room temperature. An obvious advantage of nano scrolls is that both sides are accessible (in nanotubes only the outside surface is within reach), making it possible to store hydrogen as an alternative to fossil fuels. As ordinary carbon surfaces *adsorb* (stick to surface) hydrogen, carbon nano scrolls could be used to store it. The high surface area of nano scrolls is an advantage for storing hydrogen. Nano scrolls can also be used for making light but strong materials for cars and planes.

Researchers have also grown what are known as carbon nano pipettes. Their length varies from a few hundred nanometres to a few micrometres with an inner diameter of 1–20 nm. Both the ends of the pipettes are open and the hollow internal core is rigid. It is ideal for drug delivery inside the body and being ultra-thin, pipettes can be used in atomic force microscopes. They are particularly suitable for detective work inside cells.

with 30 nm diameter, could be used in several applications including biological sensors.

The range of novel nanomaterials is increasing. Besides buckyballs and nanowires, new forms such as nano crystals and nano scrolls have been made (Box 4). Scientists at the Surface Physics Division of the Saha Insititute of Nuclear Physics, Kolkata study the basic thermal properties of thin polymer films.

Key Role of Catalysts

Catalysts play a key role in producing several chemicals. Microscopic particles with a diameter of only a few nanometres and thin coatings underlie the catalysts. Researchers nowadays examine whether they could customise catalysts, with a view to enhancing their power and adding new characteristics. For example, scientists at the Eindhoven University of Technology in the Netherlands have used atomic force microscopy to image polyethylene as it grew on a chromium ion. Similar studies were reported at the American Chemical Society meeting in Boston in 2002.

Some materials that are usually non-catalytic become catalytic at the nanoscale; gold and copper, for instance, become as hard as ceramics. Gold is inert in its bulk form. But if the diameter of the particle is reduced to a few

nanometres, it catalyses carbon monoxide into carbon dioxide. Similarly, if the titanium dioxide particles in sunscreens are reduced in size, they would absorb the ultraviolet radiation without causing the side-effect of whitening.

In a recent advance, it has been demonstrated that the average shape and size of a nanoparticle can be watched during their growth in real time. Individual surface atoms can be resolved with a scanning tunnelling microscope.

Silicon, when formed into nano-sized clumps (crystals of 2 nm in diameter, for example), has been found to be an efficient emitter of visible light. Silicon is not, however, biocompatible. And it corrodes. Hence its use in biological and environmental sensors is limited. Researchers have developed a new nanoporous silicon chip with nanometre-sized holes. The new material has unique optical properties combined with the reliability and durability of plastics. The polymer structure is made in such a way that it reflects specific wavelengths from inside the body. The changes in the reflection spectrum of the wavelengths would indicate to a medical doctor data such as the status of a biodegradable suture or drug delivery.

Synthetic opals with specified optical properties have also been developed. Semiconductor-type nanotubes on the opal surface have been made. It has been reported that such tubes transmit light better, while working with lasers. This is considered useful in all optical or electro-optical communication systems.

Initiatives in India

In India, the Department of Science and Technology of the Central Government has announced a national initiative in nanomaterials. In December 2003, the Department organised an International Conference on Nanoscience and Technology in Kolkota. Several Indian researchers presented papers and posters on a wide range of nano topics under study

at various universities and other educational institutions in India. The Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore has pioneered the study and experiments in nanoscience in India. Under the guidance of the well-known scientist, Prof. C.N.R. Rao, the Centre has done world-class research in nanoscience using state-of-the-art equipment such as the atomic force microscope.

The immediate objectives of the Centre regarding nanomaterials are: (i) fully master the synthesis of isolated nanostructures and their assemblies with desired properties; (ii) explore and establish nano device concepts and systems architectures; (iii) generate new classes of high-performance materials; (iv) connect nanoscience to molecular electronics; and (v) improve known tools while discovering better tools of investigation of nanostructures.

Within a few months of the discovery of the nanotube, the Centre produced carbon nanotubes, both multi-walled and single-walled.

When carbon nanotubes were discovered as a microscopic miracle, they were found in the deposits in the arc evaporation of graphite. This method has since been improved. A direct and effective method of producing nanotubes of various kinds has been developed. The tubes were obtained by pyrolysis (carbon vapour deposits) of hydrocarbons (such as ethylene and acetylene) over nanoparticles of iron, cobalt, and other metals.

Prof. Rao and his co-workers reported (1998) a simple and low-cost route to obtain aligned multi-walled nanotubes. Later, single-walled carbon nanotube bundles were prepared at the Centre. The average diameter of the tube was 1.5 nm. Further studies of nanotubes attracted worldwide attention.

The researchers used organometallic precursors (compounds of organic substances and metals) such as metallocenes. The precursors serve as a dual source of both carbon and metal nanoparticles. The very first experiment

in this regard was successful. Multi-walled nanotubes were produced. It was followed by the production of single-walled nanotubes and what is known as aligned nanotube applications in electronic displays, particularly as field emitters and hydrogen storage, while Y-junction nanotubes could be useful as building blocks in nanoelectronics (Fig. 4.4).

The nanotubes produced in this manner are also used for preparing other types of nanostructures. Aligned carbon nanotubes from ferocene is a good source of field electron emission.

In order to increase the yield of multi-walled carbon nanotubes, vapours of an additional hydrocarbon source were mixed along with the metallocene vapour in the furnace. The use of organometallic precursor was found to be a less expensive and easy one-step route, most convenient for the production of nanotubes.

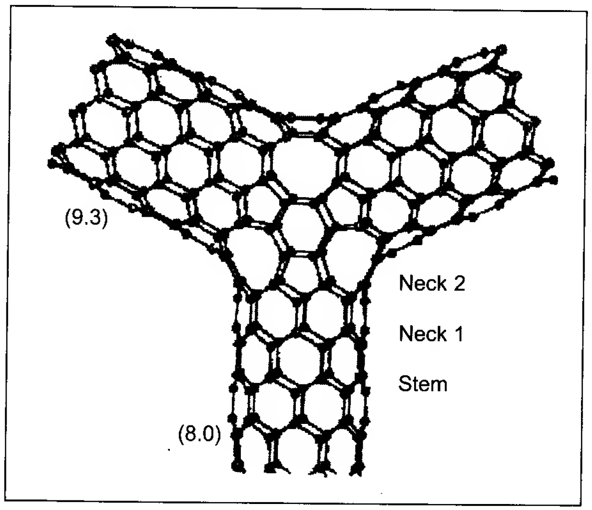


Fig. 4.4: Complex three-point nanotube junctions have been proposed as the building blocks of nano electronics. The Y-junction carbon nanotube, produced in large quantities at the Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore are considered a prototype for application in microelectronics.

The precursor route is also a good means of preparing nanorods encased in carbon nanotubes. Metals are often captured and encased to form nanorods or nanoparticles inside carbon nanotubes. Iron nanorods inside carbon nanotubes, for example, exhibit a complex behaviour. Galium nitride nanowires have been prepared involving the use of carbon nanotubes as templates.

Researchers at the Centre have shown how the electronic structures of metal and semiconductor nanocrystals differ from those of bulk materials and isolated atoms. A research group has carried out metal nano crystal research and innovations in AFM instrumentation. Metal nanocrystals have been manipulated and used as switches. Nanocrystals of various metals (such as gold, silver, palladium) and metal oxides (for example, iron oxide) of definite size have been utilised in making two-dimensional arrays that organise themselves spontaneously from the solutions. Such arrays have potential applications in surface coating and recording media.

As semiconductor technology is likely to reach its limits soon, nanoelectronics provides an alternative. The possible use of carbon nanotubes in nanoelectronics has triggered wide interest. In the multidisciplinary area of nanoelect-ronics, researchers seek to utilise a single electron nanostructure (for example, nanocrystal, quantum dot, nanotube) and to use assemblies of nanostructures for electronic, optoelectronic, chemical and other applications.

Y-junction Nanotubes

Three-point nanotube junctions were suggested as the building blocks of nanoelectronics. It is thus important to connect nanotubes of different diameters and chirality (the angle at which they are rolled). Y- and T-junctions have been considered prototypes. The Centre has produced Y-junction nanotubes in large quantities. This is a significant

achievement as spectroscopic studies in a scanning tunnelling microscope have indicated the possibility of Y-junction functioning as a diode. The findings indicate the potential for assembling carbon nanotubes in the production of computer chips.

The Centre has made nanotubes from inorganic materials too. These include niobium sulphide, niobium selenide and tungsten sulphide, molybdenum trisulphide and hafnium. The nanotubes from these materials are technologically important and have applications ranging from solid lubricants to superconductors.

Computer-controlled scanning probe microscopy enables a real time, hands-on nanostructure manipulation. Nano manipulators have been used to operate in scanning and transmission electron microscopes. Researchers at the Centre have developed stable patterns, etc. of nano crystals using the cantilever tip of the atomic force microscope (AFM). Known as dip pen nanolithography, the process involves the transfer of matter coated on the tip of the AFM to the substrate below. The patterns are densely packed and are proved to have potential applications as conducting links in nano circuitry.

Nanowires from Various Materials

The Centre has been making a variety of inorganic nanowires since the year 2000. It has made nanowires from many materials by using a relatively simple method of combining them with different forms of carbons and then heating them. The materials cover a wide range: zinc oxide, aluminium oxide, gallium oxide, indium oxide, silicon oxide as well as nitrides such as aluminium nitride, boron nitride and silicon nitride. In the case of gallium nitride, the researchers were able to obtain useful optical and magnetic properties by doping the material.

The Centre has also prepared nanorods by templating

carbon nanotubes. The rods have diameters in the range of 10–200 nm. Nanorods of selinium were made at room temperature using an aqueous medium. High yields of nanowires were obtained.

Nanowires, nanorods and nanobelts constitute an important class of nanostructure. They are studied to discover the relationship between the electrical, optical and other properties of materials on the one hand and their dimension and size on the other.

Nanoparticles: Studies in Bangalore

The Indian Institute of Science, Bangalore is actively involved in the study of nanotechnology in its various departments. The Solid State and Structural Chemistry Unit of the Institute is engaged in research on semiconducting nanoparticles since the early 1990s. Researchers of the Unit have been able to control the size of nanoparticles and study their electronic and optical properties, as a function of the size of the nanoparticles.

The basic aim of the Unit is to study the fundamental processes through experiments. The researchers have prepared and controlled the size of cadmium sulphide, zinc sulphide, lead sulphide, cadmium selenide, zinc selenide and zinc oxide nanoparticles.

The size of the nanoparticles can be varied from 1.5 nm to 7 nm. The Unit has the distinction of being one of the first to report on the details of the electronic structure of nanoparticles. The detailed electronic structure has been elucidated.

A group in the Unit has been able to combine high-quality chemical synthesis and experimental skills with extensive theoretical investigations. The group has synthesised various doped nanoparticles by mixing the materials with cobalt, copper, manganese, etc. Doping has been found to yield useful electronic and optical properties.

The group uses a wide range of techniques based on transmission and scanning electron microscopes, low and wide angle X-ray diffraction, Raman and infrared spectroscopes. Using photoelectron spectrometer, the researchers have studied the pattern of electronic structure in nanoparticles. The pattern is studied when the electrons are ejected under ultraviolet light or X-rays. The researchers could estimate and control not only the individual particle size but also the electronic structure of different materials. Based on their findings, the researchers alter the composition of their samples and evaluate the variation in size, shape and inter-particle separation distance in materials.

It is known from basic quantum mechanics that the energy level spacing or the band gap in materials increases as their dimension is reduced. It is possible to 'tailor-make' materials with varying band gap as a function of size. The research is significant because electronic devices with different band gaps have different applications. For example, telecommunications need very low band gap in the infrared region; biological applications require fluorescence in the green region (avoiding the ultraviolet rays that may destroy biological molecules). Similarly, fluorescent displays in ultraviolet, visible and infrared need different band gap materials. Manipulation of the band gap of certain materials would make them suitable for use in solar cells.

Following the preparation and analysis of various nanoparticles, the group has demonstrated their utility in devices such as a photon (light) sensor based on cadmium sulphide. Basically they shine light on certain materials and get current. Research in this field is continuing. Some of the projects are aimed at preparation of high luminescent nanoparticles with different luminescence wavelengths, understanding the growth mechanisms of the nanoparticles and preparation of different shapes of nanoparticles such as spheres, rods and pyramids.

The Department of Physics of the Indian Institute of Science is also actively enagaged in the study of nanoscience. It reviews the structural, electronic, vibrational and mechanical properties of single-wall carbon nanotube bundles. Its studies and experiments have validated the predicted remarkable mechanical resilience of the nanotubes. The Department has also conducted studies using an atomic force microscope. The Department has collaborated in an interesting experiment which proved the possibility of generating electricity from tap water (*see* Chapter 8).

The Metallurgy Division has done several experiments on nano-sized particles dispersed in a matrix, called nanoembedded materials or nanocomposites. They represent a new class of nanoscaled materials. It was found that the reduction of length scale and introduction of interfaces greatly influence the stability and transformation behaviour of metals. Many industrially useful processes have made use of this feature.

The Indian Institute of Chemical Technology, Hyderabad, is reported to have developed synthetic peptide-based carbon nanotubes (*see* Chapter 7).

Work at the National Chemical Laboratory

The National Chemical Laboratory (NCL) and the Agharkar Institute, Pune have also done outstanding work in various aspects of nanoscience, especially in the area of interface with biology. Many processes for synthesising nanoparticles often involve the use of toxic chemicals.

It is known that in Nature, many organisms produce the most exquisite inorganic nanostructures. Scientists have explored the possibility of making nanoscale metals, sulphides and oxides by utilising suitable micro-organisms (e.g. diatoms, bacteria, yeast, algae, fungi, etc.). Called ecofriendly nano factories, the micro-organisms provide a viable alternative to the physical and chemical methods

currently used for the production of nanomaterials.

Traditionally bacteria have been used in the synthesis of nanoparticles. In an unconventional method, a group of scientists at the National Chemical Laboratory has used fungi to grow nanoparticles of different chemical compositions. The group has synthesised nanoparticles without toxic chemicals by using biological systems.

The group's special emphasis is on nanomaterials at the interface between chemistry and biology. The group investigates the synthesis, assembly, properties and commercial application of nanomaterials. The core team comprises physicists, chemists, biochemists and molecular biologists to do research on nanobiotechnology. One of the aims of NCL is to develop, synthesise and assemble new nanomaterials for commercial application.

The scientists examined about 200 different kinds of fungi and selected some good candidates for synthesis of metal and metal sulphide. The group found that the use of different kinds of fungi (e.g. *Verticillium sp*, and *Fusarium oxysporum*) has led to the synthesis of silver and gold nanoparticles. It was found that the fungus acts as an important source of enzymes needed to catalyse specific reactions leading to the formation of nanoparticles. Using the fungi-secreted enzymes in a pure state is a major advantage, as it helps in synthesising nanoparticles of different chemical composition, shape and size. The process can be easily scaled up making the production of nanoparticles economically viable and environmentally friendly.

The group has also formed extremely stable quantum dots of cadmium sulphate using the fungus, *F. oxysporum*. The scientists are evaluating other micro-organisms. Efforts are under way to extend the current approach of using fungi to derive metal sulphides to other chemical composites such as oxides and nitrides, and modulate the size and shape of

the biosynthesised nanomaterials. Another group has used neem leaf extract to make biogenic metal and bimetallic nanoparticles. There is a growing interest in using ecofriendly biological methods for synthesising metal and semiconducting nanoparticles.

The Nanotech Research Lab at the Centre for Advanced R & D, Allahabad, has worked on exploiting lichen biomass as a 'nanofactory' for producing nanoparticles potentially useful for natural nano drugs. This too is an environment-friendly procedure for making nano products.

5

NO MORE MOORE'S LAW?

All the written words of history could fit on a cube of material measuring just one-hundredth of an inch wide, if the words were written with atoms.

—Richard Feynman

Transistors are electronic devices that can act as switches. They regulate the flow of electrons through electric circuits. Wired together they form logic gates and serve as building blocks in microprocessors and computers. Cramming more and more transistors increases performance as well as complexity. Over the years, the electronic circuits have shrunk to atomic scale dimensions, following advances in microelectronics, photolithographic techniques and related fields. As a result, the density of electronic chips has increased as well as their switching frequencies. One result of this trend can be seen in personal computers, which are today as powerful as those owned by governments and large corporations only a few years ago.

The integrated circuit (invented in 1958) can today take one billion transistors. It would soon have a trillion (million million) of them. Two more decades of miniaturisation of silicon semiconductors are possible, provided nanotechnology is mastered and applied.

Dr Gordon Moore, co-founder of Intel, the largest manufacturer of computer processor chips, predicted in 1965, just six years after the invention of the integrated

circuit; that the number of transistors per circuit would double every year. The doubling cycle was later changed to 18 months. His prediction is known as Moore's Law (Fig. 5.1). As the density of the transistors on a chip doubled, the process resulted in declining prices and increasing efficiency, contrary to the prediction (not really made by Moore but by Arthur Rock, an investor in Intel) that the costs of semiconductor tools would double every four years. Thanks to the rising productivity, the semiconductor industry has followed Moore's prediction for nearly four decades, though the cost of fabricating the chips has doubled every three years. Several innovations are under development by Intel and others to extend the validity of Moore's Law (Box 5).

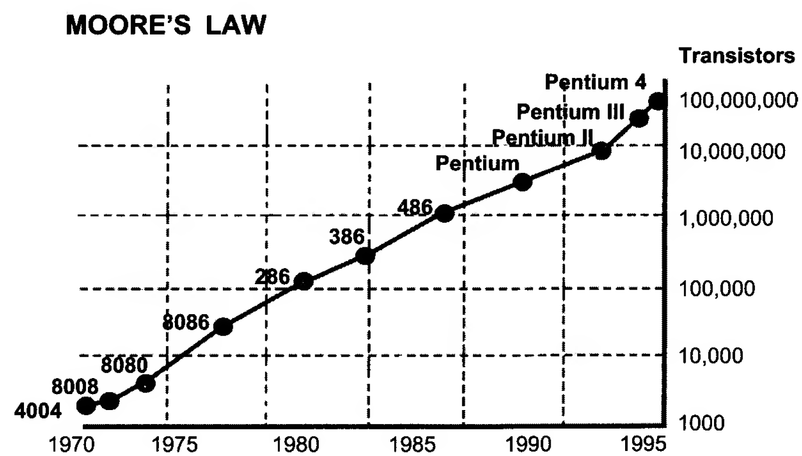


Fig. 5.1: Processing power of transistors (measured in millions of instructions per second or MIPs) has gone up because of increased transistor count. The growth has followed Moore's law, which has been driving a doubling of computing performance every 18 months. The nominal feature size of the devices has been shrunk from just under one micrometre (about one-hundredth the width of a human hair) to a minimum of less than 100 nanometres.

Box 5

Moore's Law in Action

Dr Moore predicted in 1965 that the number of transistors on an integrated circuit could double each year for the next decade. There were only 30 transistors on a chip when Dr Moore made the prediction. Moore's colleague, Prof. Carver Mead, called the prediction 'Moore's Law'. It is not a scientific or natural law but an intuitive forecast on the exponential improvements envisaged as the result of advances in semiconductor technology. Moore later changed the doubling period to 24 months but in the late 1980s, it was predicted at 18 months.

Intel, co-founded by Dr Moore, has emerged as the largest chipmaker in the world. Its first microprocessor introduced in 1971 had 2250 transistors. The number of transistors on the chip went up to 65,000 in 1975. By 1989, Intel's i486 processor had 1.4 million transistors. Pentium-4 introduced in 2002 had 55 million transistors on a silicon chip the size of a fingernail. Microchips would soon have nearly 100 million transistors on a credit-card size silicon. Intel hopes to produce a chip with one billion transistors by 2007.

The speed of the chip has also increased considerably. The i486 ran at 25 megahertz (MHz) while Pentium-4 raised it to 2.2 gigahertz (GHz). The predicted billion-transistor processor is likely to run at speeds of 20 GHz.

The range of performance has also widened. Microprocessors today run numerous gadgets from toys to colour printers and computers, besides sustaining the Internet.

The structure of transistors continues to shrink. About 15 years ago, the transistors were quite big by today's standards. The physical gate length (which controls the flow of electricity) was longer than 1000 nm and the physical gate oxide thickness was less than 20 nm. Today the gate length is less than 70 nm and the oxide thickness is 1.5 nm. Even smaller features are coming up. In June 2001, Intel announced it had developed transistor features that are just 20 nm in size, which are almost a third smaller and 25 per cent faster than the previous fastest transistors. By the end of 2001, Intel had achieved another

breakthrough—the world's smallest transistor with a gate length of 15 nm.

There is a phenomenal decrease in the price paid by the consumer too. In 1965, a single transistor cost $5, while today one can get 5 million transistors for the same amount. A new version of Pentium-4 processor chip called 'Prescott' was announced in August 2002. Its speed of operation was 4 GHz. The individual components just 50 nm across marked a turning point from microelectronics to nanoelectronics, made lithographically with ultraviolet light of 193 nm wavelength.

Continuation of Moore's Law is sought through various strategies. One strategy is shrinking the geometry of the chip from just under one micrometre to less than 100 nm as the minimum size. As the physical limit of the atomic structure is approached, Intel has demonstrated transistors with some features as thin as three atoms. Nanostructures will emerge, though they will pose problems in terms of power, heat and particle behaviour. Printing of smaller features requires shorter wavelengths of light, as the minimum feature size is determined by the wavelength of light. Hence, optical wavelength is succeeded by extreme ultraviolet light. A given wavelength can only make features half its length. Optical lithography, used now in volume production to photo-etch the chips, is called a 130 nm process. In 2002, Intel introduced a 90 nm process that allows printing of individual lines smaller than a virus. The patterning of the lines in the chip may become smaller than 50 nm if extreme ultraviolet light is used. And by 2010 the packing tolerance is expected to reach 32 nm. Intel has shown the ability to make transistors with gates as small as 15 nm in length, which will enable the production of billion-transistor microprocessors, operating at less than 1V by the second half of the decade.

As the transistors shrink in size, power consumption and heat emerge as problems limiting the continuance of Moore's Law. New structures and materials to optimize power use are under development. The new features will be incorporated in Intel's TeraHertz transistor (as announced in November 2001). The experimental device can turn on and off a trillion times a second. A note from Intel states that it would take you more than 15,000 years to turn a light switch on and off a trillion

times! The production of such devices is subjected to a mind-boggling 176 quadrillion (a quadrillion is one followed by 15 zeros) cycles of tests at the design stage.

Moore's Law will last for at least one more decade, if not longer. But it will go beyond transistors. It will integrate new devices that deliver entirely new capabilities. The steps to achieve them include increasing the transistor count, increasing their complexity and convergence of micro features such as radio frequency for mobile systems. Intel's Terahertz transistor is based on silicon. The emergence of carbon nanotube will probably be integrated into a standard silicon chip.

The impact of Moore's Law will extend to technologies such as wireless connectivity, optical transmission and processing, besides biological applications.

As Dr Moore himself says, "The most exciting thing is going to be the surprises I cannot predict. Things go much farther than you would even believe".

New Techniques

Bell Labs (US) has, for instance, pioneered some significant techniques beyond the use of photolithography to etch tiny features on silicon chips. The new techniques use X-rays, extreme ultraviolet and electron beams to fabricate high-density chips. Bell Labs has produced the world's smallest vertical transistor that is 50 nm wide. It is about 2,000 times smaller than the width of a human hair. It is known as a vertical transistor, since all its components are built on top of a silicon wafer. It has two gates to switch the current on and off, as against one in the conventional version. It could nearly double the processing speed of some silicon chips. It has another technical advantage: a leak-proof insulating layer between the transistor's gate and the channel through which current flows. As a result, the vertical transistor could increase its processing speed.

Following the discovery of plastics as electrically conductive materials, lightweight transistors have become

possible. Bell Labs has pioneered the production of plastic transistors as an alternative to silicon-based counterparts.

Smaller and Smaller Circuits

Electronic circuits are built by photolithography. The process creates intricate patterns that define integrated circuits on silicon wafers by shining light through an etched photo mask. The smaller the pattern, the shorter is the wavelength of light required. In today's commercial production, light of about 130–193 nm wavelength is projected through masks that have intricate circuit diagrams. The transmitted pattern of features is reduced by a series of refractive lenses. The final image is reproduced in thousands of silicon wafers and processed into integrated circuits.

Optical lithography can reduce the features to 130 nm across. For example, Intel's current (2003) lithography technology used in volume production is in fact a 130 nm process. The most advanced logic manufacturing technique yet is a new 90 nm process unveiled in 2002. The 90 nm width is considered a major milestone, a symbolic barrier, as it opens the way to eventually make transistors with atomic level dimensions. Smaller transistors mean more of them can be fitted into the chip and the current needs to travel a shorter distance. As a result, more intelligence could be built in and new services provided. For instance, a mobile phone can translate English into another programmed language.

Further downsizing of transistors is possible with the use of extreme ultra-violet light technology now being developed. It uses reflected rather than direct light and has a wavelength of 13 nm, some 15 times shorter than the wavelength used now, and makes it possible to have patterns of lines smaller than 50 nm.

A new process, called laser-assisted direct imprinting, has made it possible to make silicon transistors in a quarter of a millionth of a second, as against 10–20 minutes taken

now for the traditional etching. The technique was hailed as a breakthrough of the year 2002. But the appetite for smaller and smaller features seems to be unlimited! If computer-operating speeds of 10 Giga Hertz (GHz) and above are required, then circuit patterns as small as 30 nm would be needed. This is possible if extreme ultraviolet light is used for chip-making. Further miniaturisation using X-rays will have wavelengths too small to be useful in conventional photolithography. Basically a new technology is needed, as otherwise miniaturisation will slow down.

Extreme ultraviolet lithography has been used to create features that are 80 nm across on silicon wafers. This would boost the speed of the integrated circuits from 1.5 GHz today to 10 GHz by 2005. However, the size of the components in an integrated circuit cannot shrink indefinitely. Dr Moore himself points out that no physical quantity can continue to grow exponentially forever. The properties of fundamental materials would impose a limit on their reduction. Thermal noise increases as circuits become smaller. If the insulating layer in the transistor separating its gate from the channel becomes only a few atoms thick, silicon does not shut off current leakage. This causes concern. For instance, Intel's latest 64-bit itanium processor will have 410 million transistors on a single chip, radiating 130 watts of heat if run continuously. As transistors switch up to 10 billion times a second, the metal interconnects could break down. The narrower the metal wire, the longer it takes for a signal to go through. Thin films are being developed to replace the silicon dioxide insulation now being used in the chip. New materials on a nanoscale are therefore sought after.

When conventional silicon-based microelectronic components reach the features of the size of about 10 nm, carbon nanotubes with a typical diameter of 1–20 nm could be considered in their place. Carbon nanotubes are suitable for

microelectronics applications as they have high current capacity, high thermal conductivity, mechanical stability and resistance not dependent on length. Single-walled nanotubes have reasonably large *band gaps*. This phenomenon, called band gap, is a range of energies in which electrons are blocked from going through a semiconductor and helps in controlling the flow of current. In a semiconductor, the gap indicates a measure of the amount of energy it takes to move an electron from the so-called valence band (when electrons do not conduct electricity) to the conduction band in which they can transport current. However, the band gap of carbon nanotubes is not uniform, as the circumference of the tubes is not the same in all of them. As the band gap in a nanotube depends on the tube's diameter, researchers have prepared nanotubes with specified band gaps. This makes it possible to use carbon nanotubes in a wide range of electronic applications. Researchers have found that as the band gaps varies, different nano devices can be made, such as diodes (that allow flow of electricity in one direction).

A carbon nanotube can conduct, semiconduct or insulate electrons. With the availability of tunnelling microscope and atomic force microscope, it was found that nanotubes (self-assembled nanoscale structures) could be good emitters of electrons and that they can be used to conduct electrons between the transistor source and drain. Bonds among carbon atoms are stronger than any metal and so they can transmit enormous current. Copper or gold would simply melt in a similar process. Carbon nanotubes emit electrons at lower voltage than do electrodes made of other metals. Nanotubes have such tiny tips that even some tens of volts per micrometre were found adequate to release electrons. As the electrons move without resistance, carbon nanotubes are called ballistic conductors.

A Prediction Comes True

Carbon nanotubes' semiconducting properties were envisaged in 1992. A US professor, Gene F. Dresselhaus and her husband, Mildred, and Noviaki Hamata of NEC, Japan independently predicted that carbon nanotubes could be either semiconducting or metallic, depending on its geometric features. The scientists uncovered an unusual twist in the nanotubes, which determined whether it is a semiconductor or not. If a row of hexagons is found straight along the tube's long axis, the tube behaves like a conducting metal. If the hexagons formed a helix, then the tube can function as a semiconductor (Fig. 5.2).

A typical metal oxide field effect semiconductor (MOFET), first made in 1960, today contains more than one hundred million electronic components and the speed of the circuits has increased up to one giga hertz. But the increased density of transistors poses additional power demands and other problems. Carbon nanotubes could provide a solution by replacing MOFETs (Fig. 5.3).

In 1998, C. Dekker of the Delft University of Technology, the Netherlands, made the first nanotube-based transistor. An electrode placed above the carbon nanotube with

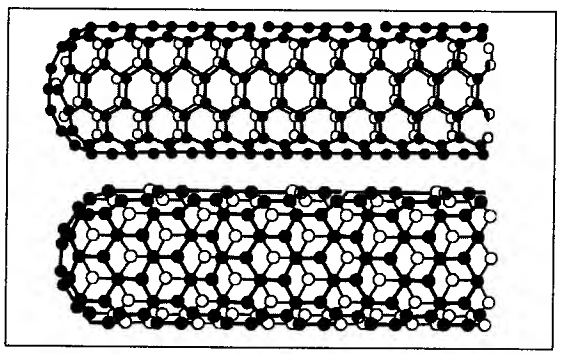


Fig. 5.2: A nanotube works like a conducting metal (top), if its row of hexagons is found straight along the tube's long axis. It works as a semiconductor, if the hexagons form a helix (bottom).

very thin insulating layers controlled the flow of electricity. It has since been found that nanotubes may one day replace silicon in semiconductors. Nanotubes have the potential to send electrons around the integrated circuits faster and more efficiently than does silicon. Nanotubes can also transport electrons at variable speeds.

Avouris of IBM and Dekker showed that a single nanotube could act as a transistor. Though it was difficult to make single-walled nanotubes with exactly identical qualities, multi-walled nanotubes were found good enough to emit electrons under the influence of an electrical field. Various groups of scientists have since demonstrated that single-walled carbon nanotubes can be used to make electronic logic devices at room temperature. Researchers at three US universities (Stanford, Cornell and Purdue) produced carbon-based field-effect transistors using zirconium oxide rather than the common silicon dioxide. The scientists claimed that the theoretical limit for transistors had been reached (Fig. 5.4).

Initially, researchers were unable to integrate transistors fabricated from carbon nanotubes into circuits, as the

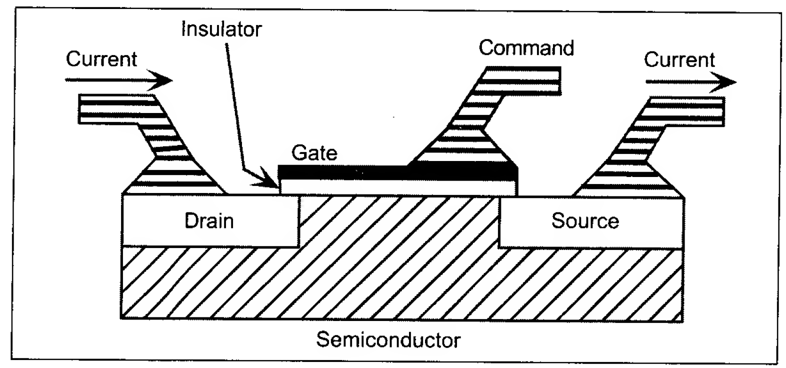


Fig. 5.3: A metal oxide field-effect transistor. A small electric current in its gate builds up an electric field in the semiconductor layer below, which then becomes a conductor allowing the flow of electrons from the source to the drain.

output voltage variations of the first generation nanotubes were too small to control the input of a second transistor—a process needed in the integrated circuit. The technique improved by 2002, when IBM's carbon nanotube-based field-effect transistors were reported to have outperformed today's silicon-based transistors. The new device had more than twice the current-carrying capacity per unit width of conventional transistors. It was also shown that the current flowing through a semiconducting nanotube could be boosted by more than five times. An IBM group has demonstrated that electrical current can be generated in a single carbon nanotube by shining light on it.

Crossing a Barrier

Even the use of a semiconducting nanotube faces an energy barrier. Known as the Schottky barrier, it hinders the crossing of electrons from the metal wire connecting the

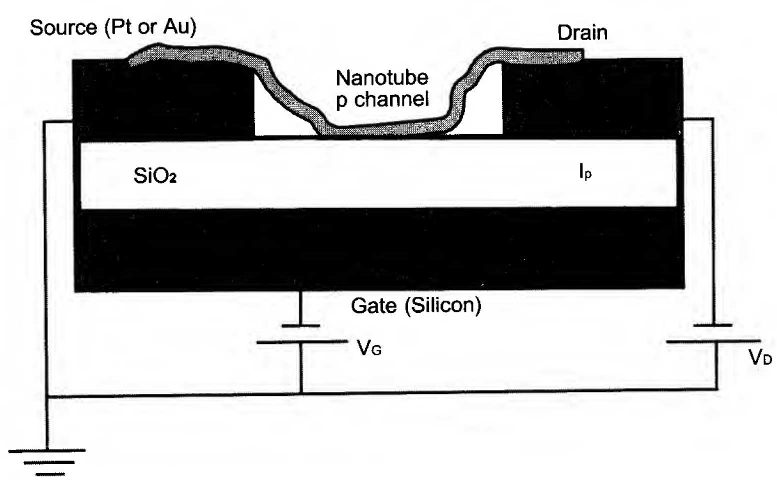


Fig. 5.4: A carbon nanotube field-effect transistor. A single-walled carbon nanotube is placed to bridge a pair of metal electrodes serving as source and drain. Field emission properties of carbon nanotubes have direct applications in microelectronic devices.

nanotube, thereby reducing the capacity to transport current. In the days of the vacuum tube, electrons from the metal wire needed heating before they could cross the barrier. In silicon and other semiconductors, recent improvements have reduced the barrier, though it could not be completely eliminated.

Recently, researchers at Stanford and Purdue universities have used palladium for the metal connecting wire. Palladium, it is reported, sticks well to the carbon nanotube. A relatively wider nanotube (with a diameter of about 3 nm) was also used. As a result, the barrier was virtually eliminated, as the electrons went through instead of being scattered in the process. This opens the way for using nanotubes for obtaining high current levels with small voltage.

An important area of research in nanotechnolgy is molecular electronics. This is based on the ability to design and synthesise molecules with electronic functionality. A single molecule can mimic the properties of a simple electronic component. This opens the way for fitting in millions of times more components in a given area. As photolithography has inherent limits in etching smaller and smaller electronic circuits, a technique called 'self-assembly' has been tried. The idea of self-assembly for programming millions of molecules using nano wires was not readily accepted, as are most new ideas. However, it was soon realised that self-assembly would overcome the prediction that the cost of new chip-making increases exponentially even as the chip features shrink.

So far, only single atoms were involved in the process of self-assembly. IBM researchers have reported (2003) that it has been possible to mix different materials and form structures with new properties. They combined lead selenide with magnetic iron oxide in a precise, programmed way. The researchers allowed the mixture to evolve a three dimensional self-assembly of nanoparticles. Lead selenide can be used

in optical communication at the typical wavelengths of 1300 and 1550 nm. The critical step in the process is said to be the choice of a correct ratio of the sizes of different compounds. The finding is significant as the process would be useful in making read heads in electronic devices.

Advances in Molecular Electronics

The size of the molecules is between 1 nm and 100 nm and they permit very high density of electronic components to be packed on a chip in a cost-effective manner. Moreover, the function of the molecule can be modified so that it can work as a switch or a sensor. This is a bottom-up approach as it builds the larger device from the molecular level, atom by atom. A scanning tunnelling microscope is utilised in the development of molecular electronics. Its sharp tip, placed at a distance from the conductive surface, is best suited to the study of single molecules.

Significant advances have been reported in the production of molecular diodes and wires based on single molecules. Prof. Luping Lu of the University of Chicago demonstrated that polymers self-assemble to form a 2.5 nm diode. It was regarded as the world's smallest diode. In a recent breakthrough, scientists have succeeded in using individual molecules to build transistors.

The miniaturisation of integrated circuits has highlighted the role of innovative imaging tools in manipulating and modelling on the nanometer scale. Nanodevices exhibit low power, high packaging densities and speed. Nanotechnology holds the promise of super dense packing of molecular scale devices quickly, inexpensively and reliably. More than the components, the connecting circuits capable of logic operations have proved more challenging. Now that nanodevices offer scope for low power, high packing densities and speed, the problem will arise not so much in making millions of them but in coordinating them

for achieving results. This calls for innovative nanoelectronic circuit architecture. Nanocircuits have been appropriately hailed as one of the breakthroughs in this field.

Semiconducting carbon nanotubes can function as field-effect transistors or as single-electron transistors. Researchers have been able to manipulate atoms and molecules to form logic gates and memory circuits. Logic circuits built out of molecules are several times smaller than silicon-based chips.

In 1999, James Tour of Rice University developed a single molecule organic switch. IBM researchers built the world's smallest computer logic circuit in 2001 using carbon nanotubes. The nanocircuit, called a two-transistor NOT gate, gave out a strong signal. The achievement marked the beginning of the transition of electronic devices from the molecular to the nanoscale.

A computer memory chip based on carbon nanotube has passed a manufacturing milestone recently. The prototype chip would store information using billions of nanotubes with a theoretical limit of 10 gigabits of data.

Researchers at the University of Toronto have invented a tiny circuit that can be started by a single electron. They demonstrated that a simple circuit could be completed, when electrons jumped from the metal tip of the electrical source to a lever coated with nanoparticles of gold. The distance between the tip and the nanoparticles was 1 nm. The single electron transistor has provided the basis for sophisticated biosensors as well. In a recent experiment, minute straws of carbon filled with spherical carbon molecules (buckyballs) were found to have excellent tunable electronic properties.

Focus on Nanostructures

Nanotubes seem to be a little off the center stage since 1998, though they continue to attract researchers. The halo surrounding them at birth about a decade ago is shifting to

nanostructures such as nanowires, nanorods or nanowhiskers. The reason is simple. Several problems have surfaced in using nanotubes in electronics. The electronic properties depend on their diameter and their crystal's shape. And control of metallic and semiconductor properties of nanotubes has proved difficult. In contrast, it has become easier to control the chemistry of nanostructures. They have been used in constructing lasers, biosensors, transistors and diodes. Scientists can alter the electrical properties of nanowires grown from a semiconductor by doping them with boron or phosphorus. Nanowires coated with charged molecules can conduct electricity and so can store information. Nanowires have been made from various materials such as gallium nitride and indium phosphide.

Nanotubes are ideal for building electron field emitters. Circuits based on carbon nanotubes do not demand vacuum or cryogenic (extremely cold) temperature to operate. The chemical stability and the mechanical strength of the tubes favour this use. Field-effect transistors were first demonstrated at room temperature in 1998. Researchers at Harvard University demonstrated a field-effect transistor based on a nanowire. Charles Lieber and his group claimed that the device's performance was comparable to that of conventional transistors.

Another breakthrough reported by Lieber is that two different materials could be placed next to each other on the same nanometre-sized crystal. This would enable nanowires to be used for almost any kind application in electronics as a building block. Carbon nanotubes as field emitters have several applications: flat-panel colour TV screens, traffic signals and display boards. Nanotube arrays have been found useful as antennas that can directly receive and transmit light waves. Lighting elements with the tubes have worked for over 10,000 hours.

Lieber and his co-workers have also made lasers that

can fit into silicon microchips. Currently lasers are too big to be integrated into chips. The first nanowire lasers, made in 2001, required light from another laser to light up. Lieber's nanowire could be switched on and off electronically.

Electronic digital logic circuits require much less space than do conventional silicon integrated circuits. It is possible to successfully downsize devices, though several leaps are required, if the technological roadblocks were to be removed in commercialising the nano products. Silicon technology today is the result of many years of successful systems engineering and materials development. The molecular electronic systems which are under development include: nano tweezers for electrical integration of nanostructures, tissue engineering, biochemical transducers, surface modified nanotubes for ideal drug delivery and optical and magnetic tagging of single molecules.

A Nano Actuator

In a significant achievement, scientists at the University of California and the Lawrence Berkeley National Laboratory have reported (2003) the making of the first-ever nanometre scale electromechanical device in the laboratory. The device is a very small 'actuator', only 300 nm long. It has a multiwalled carbon nanotube as a shaft to rotate a metal plate. The device could operate in a wide range of temperatures and frequencies in vacuum, unlike a biosensor. The synthetic device would be useful in optical, mechanical, biological and chemical systems.

Nanostructures can be used as optoelectronic devices. One such device is known as photonic crystals, produced while growing aligned carbon nanotubes. The crystals are like electronic semiconductors but conduct photons (energy visible as light) instead of electrons. Nanophotonic circuits are becoming increasingly popular in optical fibres used in telecommunication and in Internet connections (Box 6).

Box 6

Crystals of Light and Delight

A significant breakthrough in the last century was the ability to reorient the electrical properties of semiconductors so that they could perform some really useful functions. A major benefit is the emergence of transistors that have sustained the electronic revolution. Today, similar breakthroughs are required to control the optical properties of materials. One remarkable innovation is already in full bloom. Optical fibres that carry telecommunication traffic are already in place on domestic and international routes increasing the data transmission rates. The growth of the Internet demands increased bandwidth (the range of frequencies to carry telecommunications traffic). Smaller and faster components such as filters and waveguides will be necessary for processing the information.

A solution was found in what are known as photonic crystals, which can provide high bandwidth and high speed. They are like electronic semiconductors but controlling photons (energy visible as light) instead of electrons. In fact, the effect of photonic crystals in nature can be seen in a butterfly's colourful wings.

In the late 1980s, Prof. E. Yablonovitch (now at the University of California) and Prof. S. John (at the University of Toronto) independently did pioneering work on photonic crystals. It was proposed that a periodic arrangement of metallic or dielectric objects could have what is known as photonic band gap, analogous to the electronic band gap in semiconductors. The photonic band gap represents a new class of materials, where the flow of light waves can be guided; and the process is facilitated by nanoscale patterns made on photonic crystals. Photonic band gap materials can steer light beams exactly to the required place; they can slow them down or enhance and manipulate them. They can block certain photons and allow other wavelengths of light.

As laptops become increasingly wireless, nanophotonic circuits assume significance. The information from the photonic crystals has to be converted into electrons before they are transmitted on communication channels. The circuits will have electrons and photons, the former for supporting logic and memory and the latter for handling telecom links. The enhanced intelligence in the optoelectronic chips will make it possible for the user to talk to the computer. The crystals of light are designed to delight the consumer with new features such as surfing the net from cell phones.

Researchers at Kyoto University have discovered a technique of making photonic crystals channel several wavelengths of light at once through very small areas efficiently. The technique is based on adding intentional defects or areas without gaps. They used several photonic crystals making the size and spacing of gaps in a proportional way. The distance between the successive gaps becomes less and less by 1.25 nm than the previous one.

The Kyoto researchers have used the technique to separate seven slightly different colours or wavelengths of the infrared light (by just 5 nm) used for long-distance communication over optical fibres. The technique is used to make an add-or-drop device in optical communication, which is 250,000 times smaller than today's optical devices that combine and separate different wavelengths in the same channel.

Super-dense Hard Drives

The emerging nanoscale devices would call for new capability in data storage as well in the next five years. Richard Feynman's dream of storing information on an atomic scale is coming true. Scientists at the University of Wisconsin (Madison) have created an atomic scale memory using atoms of silicon; using a scanning tunnelling microscope, the scientists set atoms to represent the *ones* and the gaps between the atoms to indicate the *zeros*. The technique does not involve conventional lithography, which uses light to etch the pattern on a silicon wafer. It is claimed that the technique would provide a storage density a million times greater than a conventional CD-ROM. Commercial versions are, however, several years away.

Meanwhile, IBM's research laboratory in Zurich has reported a breakthrough. The density achieved by their researchers was one trillion bits per square inch, which is 25 times that of today's hard disks (or equivalent to data in 300 CDs). Called the 'milliped', the project provided 25 nm spacing between bit centres. An atomic force microscope was used to punch nano-sized bits on a thin plastic film to create high storage density. However, a large array of recording probes was needed, because a single AFM could operate at best on the microsecond time-scale (millionth of a second) and could not work as fast as magnetic writing heads that today record one bit of data in one nanosecond (billionth of a second).

Gigabits of Memory

New technologies are emerging that would open up the possibility of storing billions of bits of information in an area the size of a 25-paise coin. In 2002, Hewlett-Packard made use of molecules known as rotaxanes instead of silicon as memory bits. It was claimed that one square centimetre of such molecular circuitry could store 6.4 gigabits of information. Actually, about 1,000 rotaxane molecules constitute one unit, which changes its structure and hence its resistance to electricity to indicate a *one* or a *zero*. This molecular memory can be retained even when the power is off. The demonstration showed a density of memory that is ten times more than the best silicon commercially available.

Just as we find it difficult to read very small print, it becomes harder for a sensor to 'read' smaller bits of data with weaker magnetic field. Packing more and more bits would call for more and more sensitive sensors. This challenge is now being addressed.

The Colourful World of Quantum Dots

Quantum dots or nanocrystals are nanoscale semiconductor particles. Their optical behaviour depends on their size. Roughly spherical, the size and shape of these crystalline particles can be precisely controlled and hence the number of electrons they have, ranging from one to several thousand. Billions of dots can fit on a pinhead! Also, quantum wires to connect the dots are being made. Quantum dots can be considered as artificial atoms, because they have only a fixed number of electrons confined to a small area. The confined electronic structures are called by various names: quantum dots, single-electron transistors, etc. Quantum dots can be used as light emitters, photo cells, optical devices and fast optical switches.

The Materials Science Division of the Bhabha Atomic Research Centre, Mumbai has been studying various methods of forming nanocrystals. Also in Mumbai, scientists at the Indian Institute of Technology and the Tata Institute of Fundamental Research have developed techniques to produce semiconductor nano composites with ideal optical properties.

The small size of the quantum dot makes a material very different from its bulk form. Scientists have been trying to make silicon emit light efficiently in the visible range. Initially they succeeded in making the silicon dots emit red light and later green and blue ranges in higher frequencies. The scientists found that if the dot becomes smaller in size, then the emitted light moves towards blue. Larger dots emit red light. The beauty of it is that they can shine for months or even years.

The light-emitting powers of quantum dots have been found useful in luminescent materials. At the Lawrence Livermore Laboratory (US) researchers have made silicon and germanium quantum dots that emit light throughout the visible spectrum, all the way from infrared to

ultra-violet. The dots can be tuned to any wavelength over that range. The Laboratory has made light-emitting diodes from quantum dots. The dots that are excellent light emitters would be useful in all optical switches, light-emitting diodes and optical amplifiers. The dots can provide a million-fold increase in speed as against the Ethernet's speed of only 10 megabits per second. Silicon nanocrystals can also be used in quantum dot lasers, as they can send rapid pulses of light.

Quantum dots have been used in biological applications as well. In fact, observers point out that their biological application may be realised sooner than their use in electronic devices (*see* Chapter 6).

Impact on Computers

Nanotechnology will have an impact on computers too in the future. Nanostructures are ideal for computer simulation and modelling. As the size and scaling of the structure are small, there is potential for extraordinary accuracy in analysis. The first true electronic digital computer was built in 1946. It performed 5,000 additions or 400 multiplications per second, a record at that time! The computer weighed 30 tonnes, consumed 150 KW power and had 18,000 vacuum tubes. John Von Neumann and his team built the computer. Since then, four generations of computers have been made.

The next generation of computers could be based on silver nanoclusters that generate light when an electric current is applied. Each nanocluster, depending on its size, responds to very specific voltages and puts out light without the need for separate electrical connections. This is a great advantage compared with today's transistors, as their ever-decreasing scale makes it difficult to control the supply of electrons to get the light.

The fifth generation computer (2003) will be built using nano integrated circuits. Currently, technologies are

emerging to fabricate ICs with billions of transistors on a single one-centimetre unit. In future versions, the executing time, switching frequency and size will be decreased by a million times, while memory capacity is likely to be increased a million-fold.

A microscopic computer is on the cards. It is called magnetic nanite. Magnetic chips in it will be implanted into cell phones, which would then be able to send TV pictures and surf the net. What is more, in what looks like science fiction today, electronic chips the size of a few atoms can be woven into various objects including clothes! It is reported that as a result, phones, calculators and music players could be absorbed into clothing!

As a long-term goal, computer scientists and mathematicians have teamed up to explore the scope for what is known as a quantum computer. It will be designed to work on entirely new principles and is expected to be a million times faster than today's fastest supercomputers (Box 7).

Learning from Nature

The dimensions of several electronic components have become smaller than some biological structures. This has opened a new window of opportunity to integrate engineering and biology at the nanoscale. Increased knowledge from life sciences is being used to solve engineering problems, while nanotechnology has been found useful in solving problems in life sciences.

Nature's molecular systems are quite sophisticated. Complex molecular systems vary in density and relay information, carry out different jobs and above all self-assemble into complex shapes. For example, biologists and engineers are engaged in research on making memory chips based on DNA molecules, which have an inherent ability for self-assembly into ordered patterns.

Biological organisms are basically self-assembled. They

Box 7

Against Common Sense: The Quantum Computer

Heisenberg's famous uncertainty principle reflects our daily experience: if you know where exactly something is, you can't know where it is going and vice versa. But inside an atom, it is an unreal world. Common sense does not prevail! Unlike a switch in a computer which is either on or off, a switch obeying the so-called quantum mechanics can be both on and off at the same time! A quantum bit or qubit can represent one, zero or potentially any combination of one and zero. This paradox is technically called a superposition to indicate that there could be infinite number of superpositions. Based on this idea, a quantum computer could one day be million times faster than today's super computers, as superposition allows parallel calculations.

Imagine a computer working out all possible calculations at the same time. One can understand it by an example: suppose a ball is hidden in one of eight baskets; one can open the baskets one by one or all at once to speed the search. The quantum computer does the latter, unlike today's computers that do it in two steps. The technique can be applied not just to search a word in the Web in the Internet but also to break security codes.

There are real problems in realising the quantum computer. While a quantum computer is at least five decades away, a property of the electron, called spin, is considered to realise the revolutionary number crunching. An electron can behave like a magnet in spin-up or spin-down position. While the negative charge of the electrons makes the current flow in several gadgets such as toasters and computers, the electron's spin-up and spin-down positions can be used to represent the ones and zeros of digital programming. The new technology is called *spintronics*. A spintronic read head can detect very weak magnetic fields and hence potentially hard disks could hold an immensely more data. Spintronics can be used in creating magnetic random access memory (M-RAM). It has no electrical demand unlike today's desktop computers that need to be refreshed 60 times a second to keep the device turned on. Spintronics can in one day put enormous memory into computers.

An innovation that may help evolve super-fast quantum computers is the capacity to detect extremely small motion of matter (millionths of a nanogram) called the quantum limit. The motion is revealed by the changes in current caused by the movement (or vibrations) of a nanoscale beam. Such a sensor would be useful among others, to probe the tiny architecture of microchips.

begin with one cell and evolve into bigger organisms—a process described as self-assembly. The process involves 'recognition' between different elements, and binding of the elements through diffusion and other forces. Carbon nanotubes offer a new building block for the construction of molecular circuits. It is possible to acquire control of molecular structures and create materials and devices to molecular precision.

Nanoelectronics has benefited from microbes too! Mud-loving microbes have also been roped in! A team of scientists from the NASA Ames Research Centre has put such a microbe (a single-celled organism which thrives in near-boiling mud) to work on the manufacture of nanoelectronics. The team altered the gene of the microbe and added an *E. coli* bacterium that rapidly multiplied, yielding a new protein. Next, the protein (without the *E. coli* protein) was exposed to gold semiconductor nanoparticles. The process resulted in the formation of quantum dots (5 nm)—semiconductor nanocrystals—that can be of use in nanoelectronics.

Microbes and Nanoelectronics: Research in Pune

The Division of Microbial Sciences of the Agharkar Research Institute, Pune, has done significant research on biological strategies for the production of metal-based nanocrystallites. One of their works involved the synthesis of cadmium

sulphide (a semiconductor) nanoparticles by a certain yeast strain using some cadmium metal. The particles were 1–1.5 nm and structurally similar to the ones chemically made. The biologically synthesised nanoparticles were for the first time used in the fabrication of a diode (which allows the current to pass in one direction).

Biomineralisation is common in nature. The formation of teeth, bones, corals and shells shows the process in action. Several micro-organisms can transform metal ions in their surroundings into nano-sized crystallites with definite shape and composition. Recently attempts have been made to exploit biological methods for the production of nanocrystallites.

Cadmium sulphide crystallites were produced using a certain bacterium also. It was noticed that certain bacteria thrive in waterlogged soils and polluted lakes and where metals are present, they can react with them and produce metal sulphides.

Another type of bacterium has been used in producing metallic silver-based single crystals. When cultured in the presence of high concentrations of silver salts, the bacterium accumulates large quantities of silver as particles. Different types of nanoparticles can be produced using biological means. Such nanoparticles may be used to make composite structures that have controlled optical, electrical, magnetic and other properties. These are some of the characteristics needed for making better solar cells and electrical batteries, just to give two examples.

Plate I: Transmission Electron Microscope at the Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bangalore.

Plate II: Conducting Atomic Force Microscope at JNCASR.

Plate III: Researchers at JNCASR preparing carbon nanotubes using the chemical vapour deposition technique.

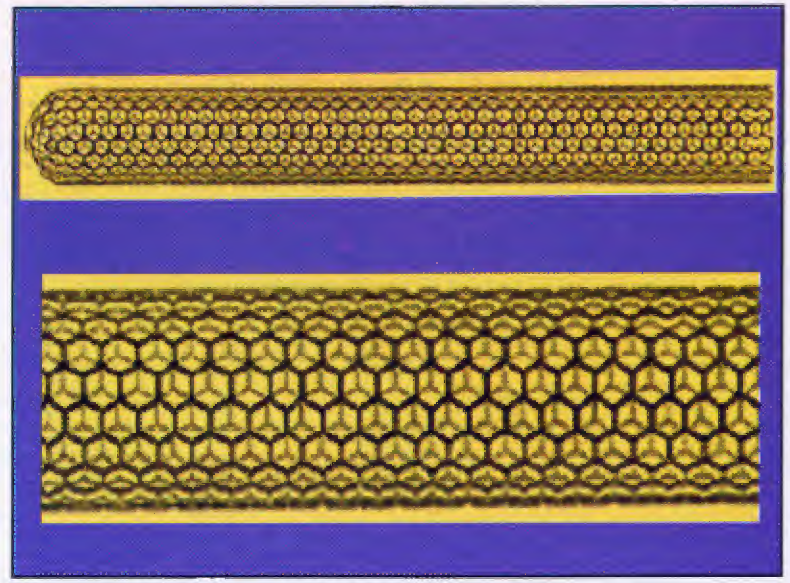


Plate IV: Carbon nanotubes (upper plate); enlarged view showing details (lower plate).

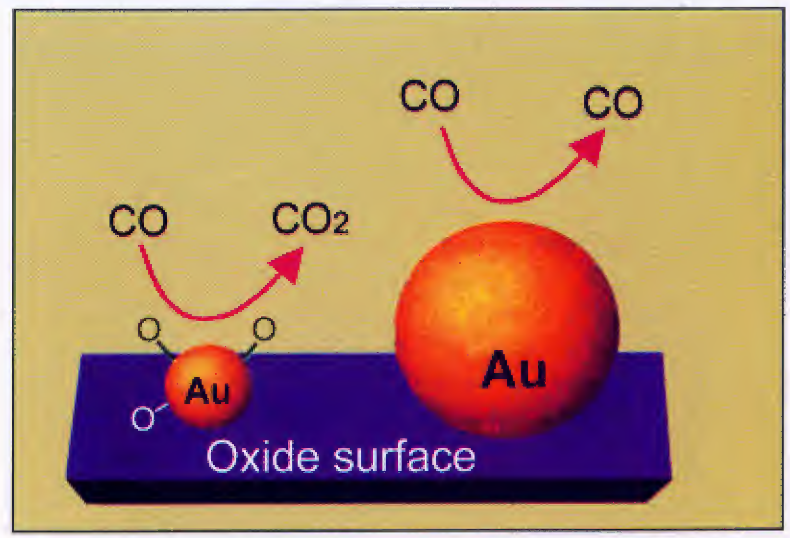


Plate V: Chemistry changes with size! Gold (Au) is inert in its bulk form, but as a nanoparticle, it catalyses CO into CO_2.

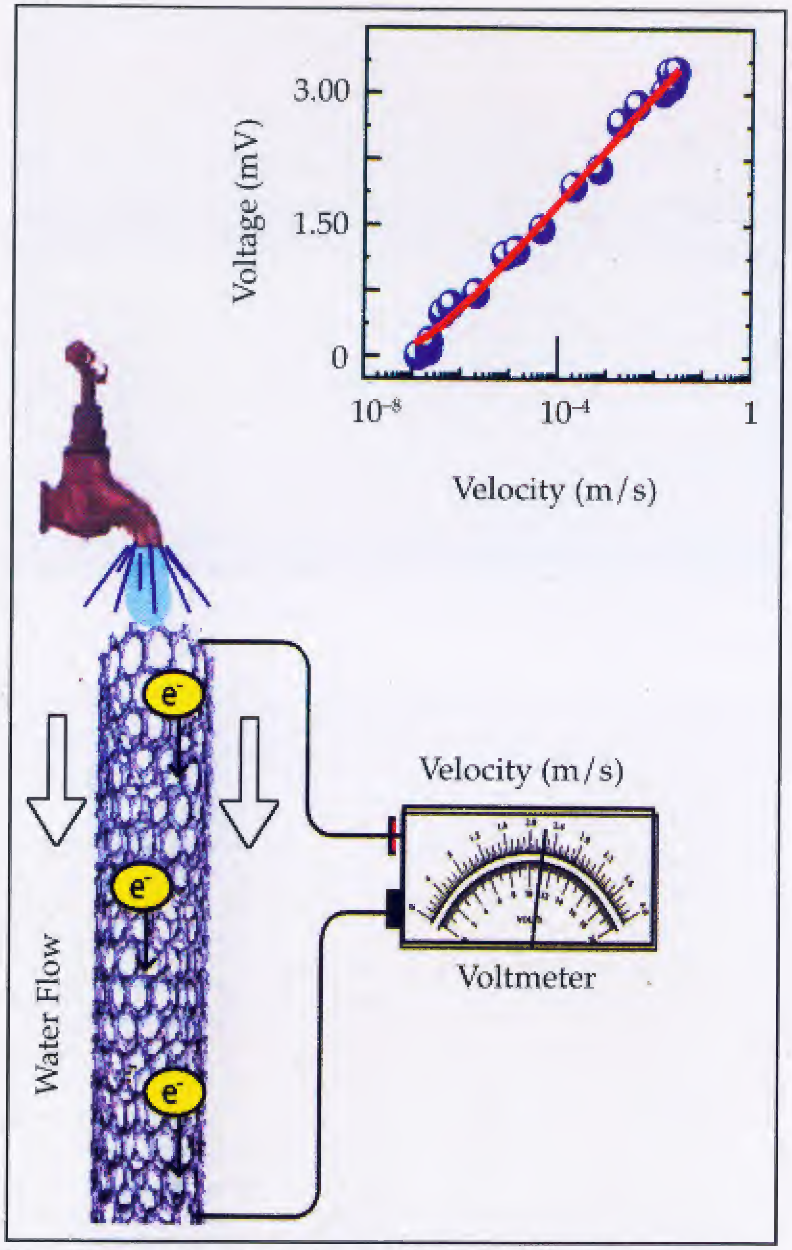


Plate VI: Scientists of the Indian Institute of Science (IISC), Bangalore proved that using nanotubes can help produce electricity from the flow of tap water.

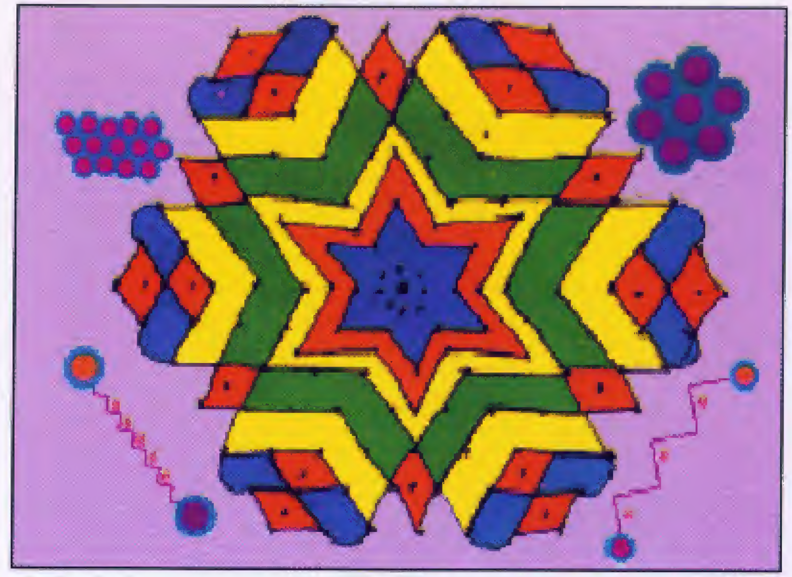


Plate VII: Researchers at JNCASR have shown how differently sized cadmium selenide nanoparticles emit different colours.

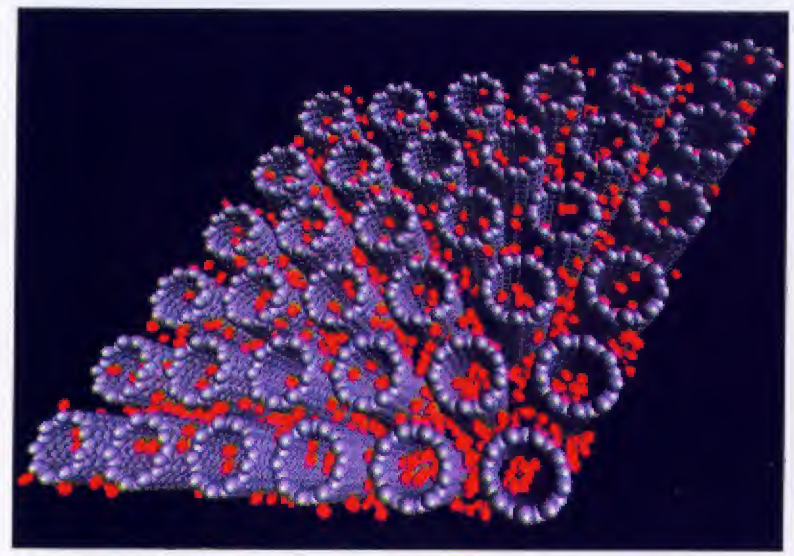


Plate VIII: Reaction of hydrogen with a bundle of nanotubes.

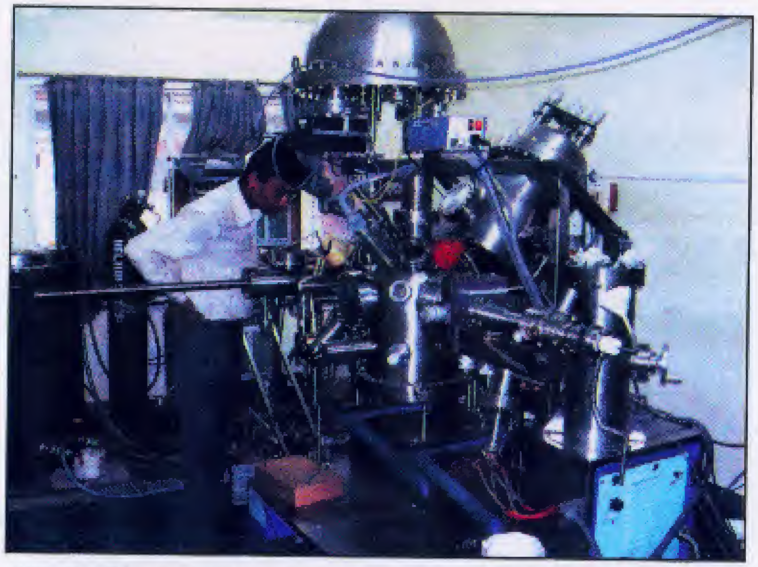


Plate IX: Photo electron spectrometer at IISC, Bangalore.

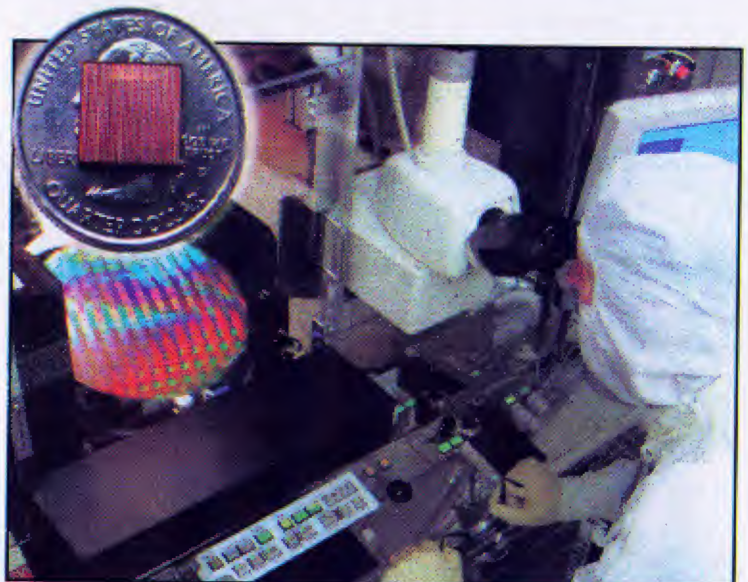


Plate X: An Intel laboratory. Already 330 million transistors are integrated into a single chip by Intel (smaller than a US quarter dollar coin) using new 90 nm process for printing intricate patterns on the chip.

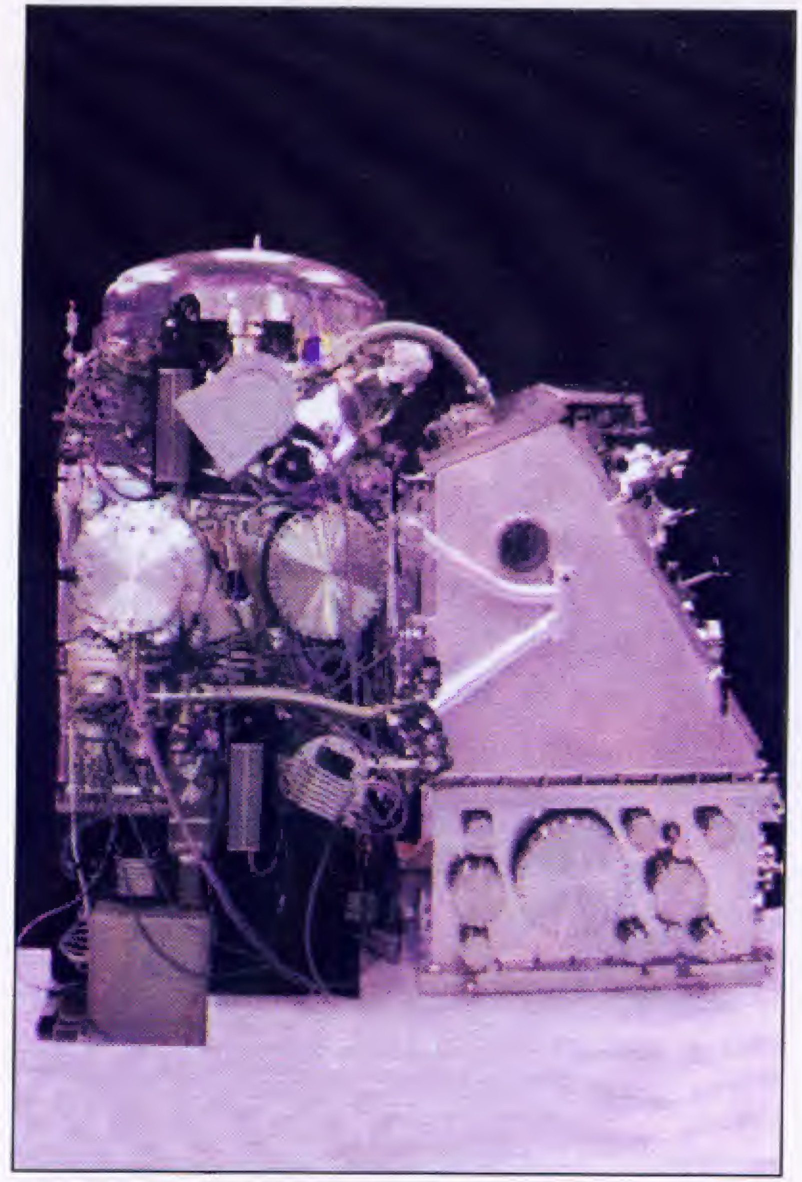


Plate XI: Extreme Ultraviolet (EUV) Lithography, currently under development, uses reflected rather than directly transmitted light for patterning lines smaller than 50 nm.

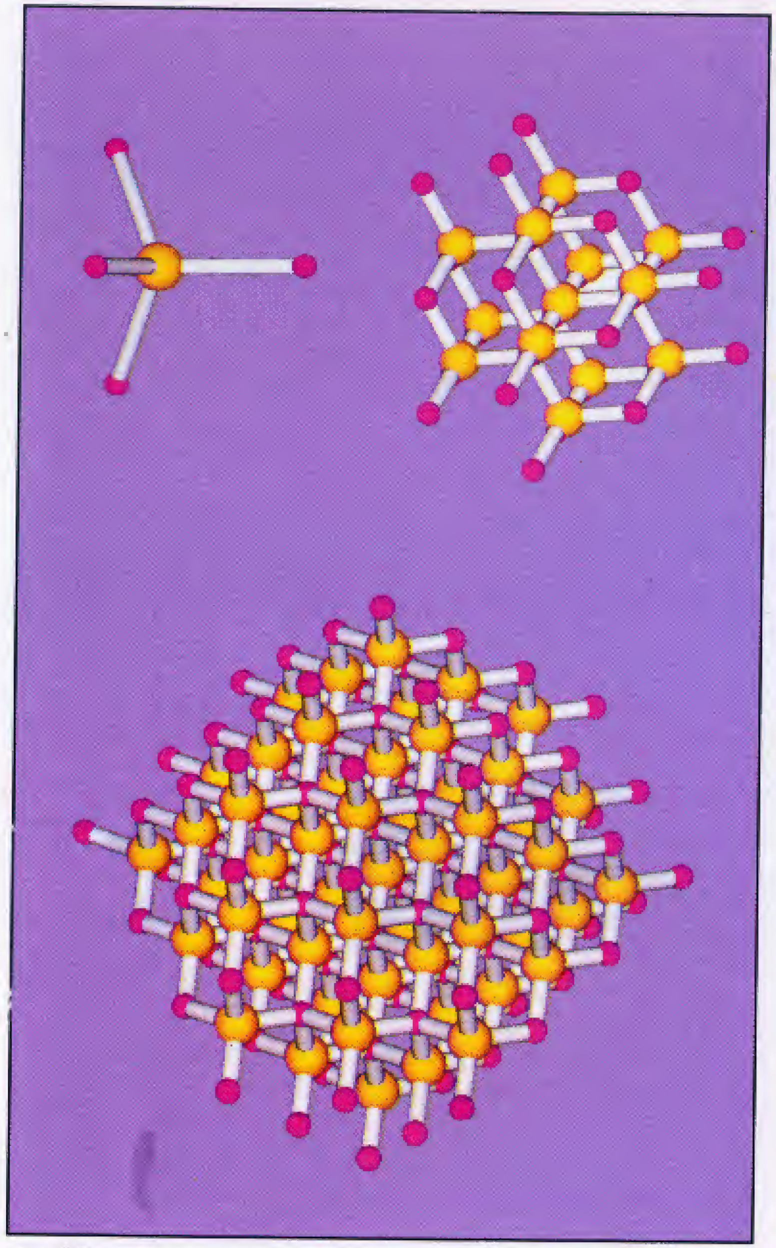


Plate XII: A computer-simulated view of the growth of zinc sulphide nanoparticles (with the central atom of zinc surrounded by sulphur atoms).

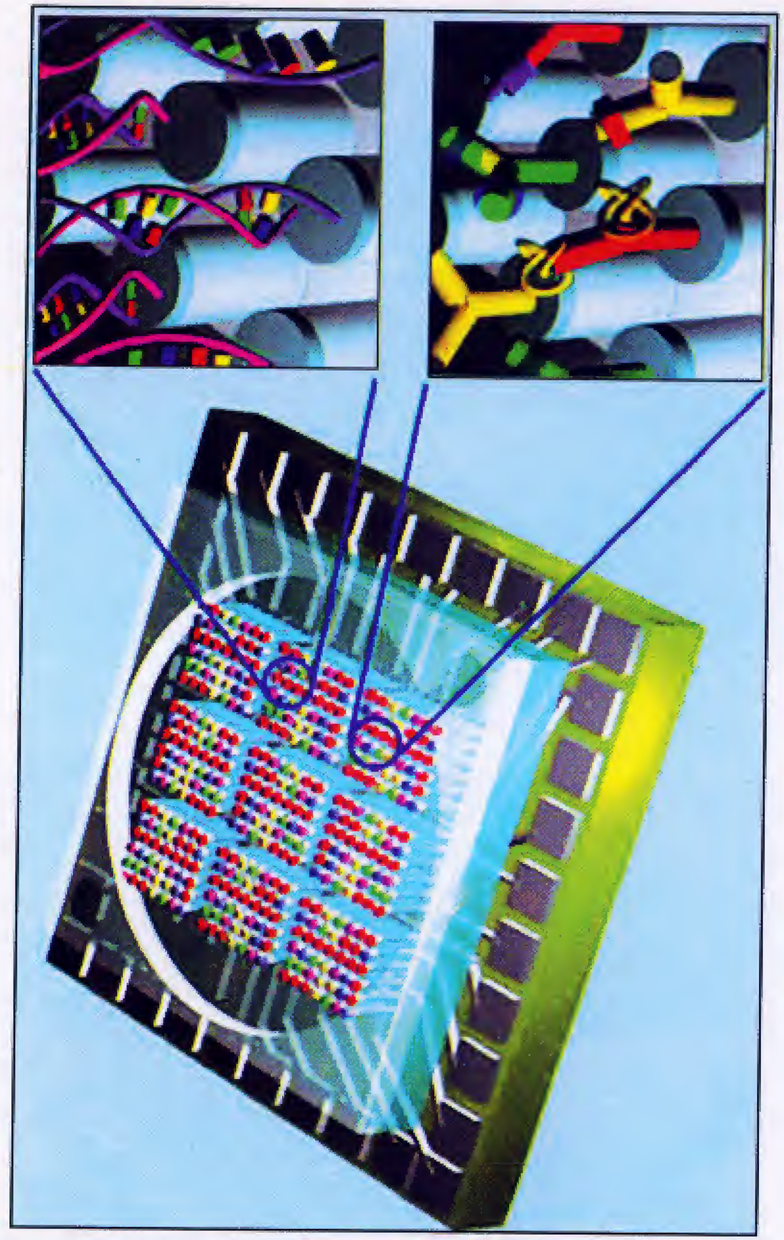


Plate XIII: In this device developed by NASA, DNA molecules attached to the ends of the nanotubes detect specific types of DNA or other substances. (*Courtesy*: NASA)

Plate XIV: Gerd K. Binnig

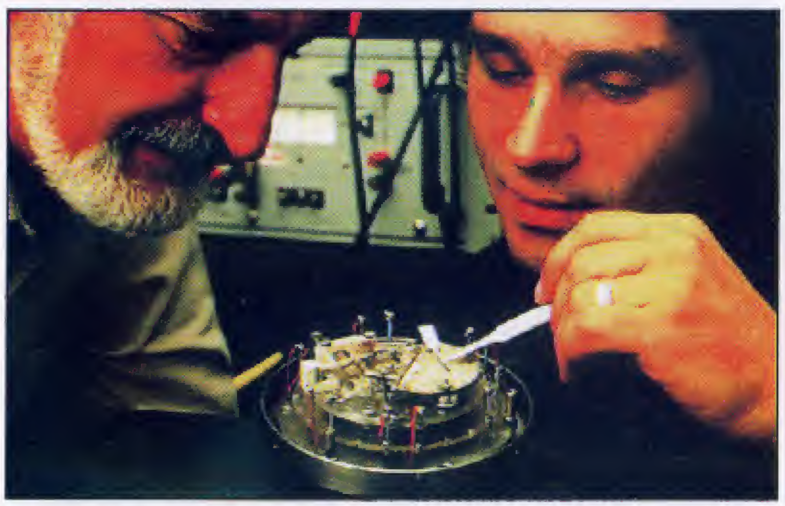


Plate XV: Heinrich Rohrer (left) and Binnig, co-inventors of the scanning tunnelling microscope.

Plate XVI: Satyendranath Bose

Plate XVII: Richard Feynman

Plate XVIII: Gordon Moore

late XX: Francis Crick

Plate XIX: C.V. Raman

Plate XXI: James Watson

Plate XXII: Maurice Wilkins

Plate XXIII: Rosalind Franklin

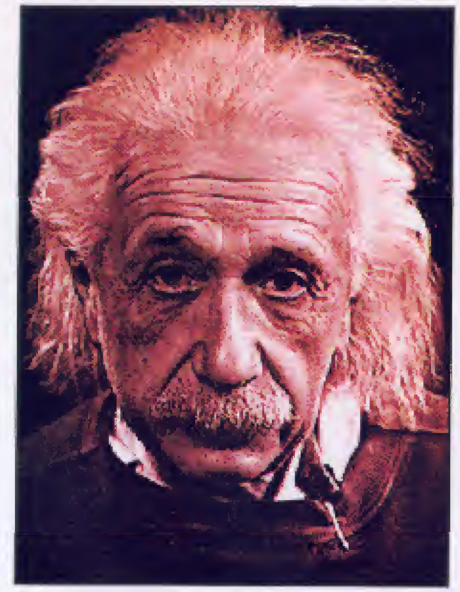


Plate XXIV: Albert Einstein

Plate XXV: Eric Drexler

Plate XXVI: Bill Joy

Plate XXVII:
Prof. C.N.R. Rao

6

DETECTIVES IN THE NANOWORLD

The biggest ethical problem we have is, not using our knowledge.

—James Watson (a pioneer of the genomic revolution)

Fascinating discoveries by several outstanding men and women over the last three centuries have revealed a lot about human biology. Increasingly sophisticated diagnostic devices provide us astonishing details about the functioning of the human body (Box 8). Yet the human body still retains its mystery and a lot remains to be discovered and understood. Nanotechnology could help reveal the hidden mysteries of the human body in more detail. There is a nanoworld within us waiting to be discovered.

Nature has an impressive variety of biomolecular nanodevices such as molecular motors and protein membranes. The cell itself is a masterpiece of nanotechnology. The completion of the human genome project has greatly enhanced the scope for research on biological systems (Box 9). Conventional modes of testing such as X-ray diffraction do not provide the details required to understand the complexities such as gene regulation and similar dynamic processes in biological molecules. Nanotechnology enables scientists to investigate the structure and functions of biomolecular systems and even manipulate the biological structures. We need better tools to measure the

Box 8

Towards the Nanoworld Within Us: A Time Line

1609 Hans Lippershey and Zacharias Janssen independently invented an improved microscope
1628 William Harvey described blood circulation in the human body
1663 Robert Hooke used a microscope to study biological matter
1676 Anton Van Leeuwenhoek observed bacteria in a microscope
1856 Lewis Pasteur explained fermentation caused by micro-organism
1857 Rudolf Virchow held that cells constituted the fundamental units of all living beings
1859 Charles Darwin published his famous *Origin of Species*
1866 Gregor Mendel indicated natural laws of inheritance
1869 Friedrich Meischer discovered DNA in the sperm of trout
1882 Pasteur observed lymphocytes in the human immune system
1892 August Weismann proposed that chromosomes were at the heart of heredity
1902 Walter Sutton showed that hereditary information was carried by chromosomes
1927 Hermann Muller showed that X-rays could cause genetic mutations
1944 Oswald Avery, McCarty and Colin MacLeod discovered that DNA was the hereditary material, a link between generations
1948 Linus Pauling proposed a theory that many proteins were helical or spring-shaped
1951 Rosalind Franklin, a crystallographer, took X-ray diffraction images of DNA
1953 Charles H. Townes invented the maser, which led to the development of the laser
1953 James Watson and Francis Crick announced the structure of DNA as double-helix structure that spells out a code
1962 Watson, Crick and Maurice Wilkins, who worked on the DNA structure, were awarded the Nobel Prize
1970 Hargovind Khorana synthesised the first man-made gene. He shared a Nobel Prize with R.W. Holley and M.W. Nierenberg for their contributions to deciphering the genetic code
1971 Albert Knudson discovered the first tumour suppressor gene; Raymond Damadian showed that tumours could be determined by magnetic resonance imaging
1972 Stanley Cohen and Herbert Boyer pioneered the recombinant DNA technology (genetic engineering)
1975 Monoclonal antibodies were developed and used in medical diagnosis
1977 Sanger and his team developed DNA reading methods and completed the first DNA sequence of an entire genome of bacteria
1978 The first test-tube baby, Louise Brown was born. At 26 (2004) she is doing fine!
1986 The Human Genome Initiative was announced
1986 Atomic Force Microscope was used for imaging non-conducting samples
1987 Pedersen, Donald Cram and Jean-Marie Lehn were given the Nobel Prize for Chemistry, which explained the feature of self-assembly, an idea basic to bottom-up nanotechnology
2000 The Book of Life (the genome) was deciphered
2003 Researchers completed the work of determining the sequence of the genetic code

activities in the cell and between them. Ingestible nano-devices as well as non-invasive testing will revolutionise medical diagnostics. Besides drug delivery, tissue regeneration, growth and repair are possible. However, nanoparticles often disintegrate in the human body before reaching the target area. Hence research is being carried out to provide the stability needed by the nanoparticles.

Box 9

The Human Cell: A Nano Masterpiece

Living cells have nanoscale structures. For a long time after humans evolved, the composition of the cells remained an unexplored mystery. A remarkable series of scientific and technological innovations starting with the optical microscope has provided deep insight into the structure of the cells. The discovery is by no means complete.

It is now known that our body has 100 million million cells. A cell is 30–50 micrometres in diameter with its nucleus of about 10 micrometres in diameter. The smallest living cells are about 0.1 micrometre in diameter. In contrast, the width of DNA is just 2 nm.

A cell is a masterpiece of nanotechnology, as its features are measured in nanometres. Its proteins are made on a nanoscale basis. A protein by the way is extremely small, measuring typically from 1–10 nm. Single molecules are identified in scanning probes.

X-ray crystallography, nuclear magnetic resonance and atomic force microscopy have revealed the incredible nature of atomic scale chemistry. The extraordinary details inside the cell show, for example, how proteins and nucleic acid machinery operate on the nanometric scale and how they are designed for muscle movement and dense data storage. Cellular nanosystems assemble themselves. Moreover, inside the cell are, what are known as, weak interactions that result in bonds being made and unmade.

A professor of physics, Paul Selvin and his team, at the University of Illinois at Urbana-Champaign, have developed an extremely accurate imaging technique for looking inside the cell and have found a strange phenomenon: molecules of myosin V that converts chemical energy into mechanical energy and acts as a cargo van within the cell. It walks like a human and does not crawl.

Again, nature builds complex molecular machinery with simple building blocks, e.g. with 20 amino acids that break up the proteins. Cells are self-replicating collections of molecular

nanomachines. Ribosomes (responsible for the translation process) in the cells copy DNA into RNA and then collect the correct amino acids to create proteins. Enzymes—protein molecules that act as catalysts—cause specific chemical reactions without changing themselves. Energy-rich molecules provide 'fuel' to cells. Molecules spontaneously fold themselves into functional three-dimensional structures.

Nanoscientists try to mimic the cells in a variety of ways, e.g. as catalysts, as mechanical movers, as energy conservators and information processors and as synthesiser of new materials. With all the modern tools, the cell's work in passing on its information to its progeny remains a wonder.

Nanotechnology enables scientists to identify millions of genetic variations among individuals and derive patterns, if any, in these variations. By simulating the oily sheath enclosing a cell's watery innards—one-1000th of a millimetre wide—researchers are trying to figure out what stimulates immune cells that fight diseases. The artificial membranes built on a nanoscale could help researchers understand what triggers allergies.

A cell membrane is dynamic, as it will decide if it will admit an ion, molecule or other substance like medicine through the cell's wall. The cell's information processing abilities have attracted the attention of researchers who plan to develop nano-, bio- and information technologies based on the biological model. The US space agency, NASA and the University of California have set up the Institute for Cell Mimetic Space Exploration. The goals include creating nano- and micro-scale sensors, energy sources, writing computer codes, astronaut health monitoring and spacecraft resource management.

The cell is an outstanding model of a self-replicating nano machine. It would be an epoch-making achievement if we could copy evolution and mimic the simple cell. While this remains a distant goal, the working of the cell itself shows the way to meet the challenge. Initially, a chemical process creates large linear molecules. This is followed by molecular self-assembly at various levels. In fact, the coded information for all these tasks is within the molecules in the cell such as DNA, RNA and proteins. Imitating them is a big challenge. Chemical and

biological sensors are being designed to imitate molecular processes in living organisms.

For the first time, scientists (at the University of Michigan) have been able to image chemical activity inside living cells in real time and three dimensions. The nano probes, 20 nm in diameter, fit inside a cell. Molecules inside the probe emit light on selected ions (e.g. zinc or copper), which are critical for cell functions such as muscle contraction. Elsewhere, scientists have found that neurons treated with nanoparticles (coated with atoms of cerium and oxygen) bound themselves to free radicals that otherwise damage the cells and induce ageing of the cells or cause age-related disorders.

The Human Genome on a Nanoscale

A discovery of profound significance in understanding the unit of heredity is the chromosomes. Each of the estimated 100 trillion cells has a total of 46 of them, including those indicated by the gender (Fig. 6.1).

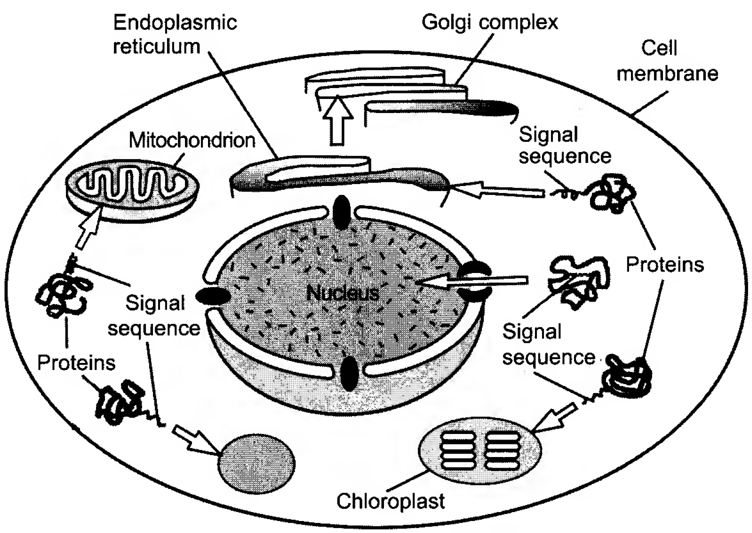
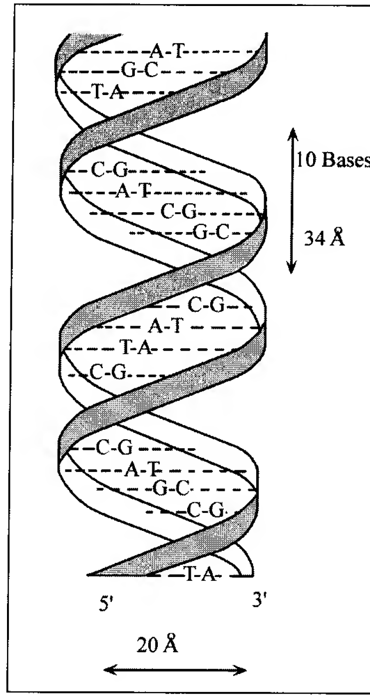


Fig. 6.1: Our body contains 100 million million cells. The nucleus of cells contains chromosomes that store our genetic code. Each cell is a masterpiece of nanotechnology.

Fig. 6.2: Tightly coiled up in a chromosome is the long thread-like molecule called deoxyribonucleic acid (DNA). The DNA molecule has a twisted ladder-shaped structure (double-helix). Each rung of the ladder is a letter or base of the genetic code: *C, G, A* or *T* (which stands for cytosine, guanine, adenine and thymine). A full rung consists of a pair: *A* always pairs with *T* and *C* goes with *G*. A sequence of letters spells out a gene. Hydrogen bonds hold complementary base pairs. which are 0.34 nm apart axially. There are ten of them within each full turn of the double helix, which is 3.4 nm long.



Another discovery that proved vital to our understanding of the transfer of information by the cells is the famous double-helix structure of the deoxyribonucleic acid (DNA). The structure, proposed by James Watson and Francis Crick in 1953, is a sequence of chemical bases that spells out a code passed on from generation to generation (Fig. 6.2).

Hydrogen bonds that hold complementary base pairs display remarkable regularity measured in nanometres (Fig. 6.3). It is now known that DNA is ideally suited to be a building block on a nanoscale, as its base sequences can be programmed to self-assemble into complex patterns.

The order of the bases is the blueprint of a gene for making proteins, the building blocks of life. In each of the cells that make up our bodies, a copy of the body's blueprint or genome is present. Decoding DNA or determining

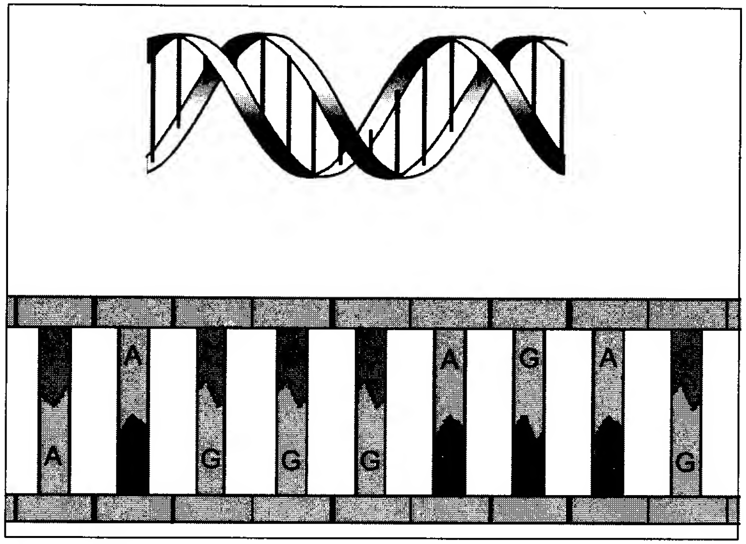


Fig. 6.3: Three-letter words in the genetic code specify amino acids. The top layer above, for example, reads TACCCAGAC, which stand for three amino acids, viz., tyrosine, proline and histidine, respectively for incorporation into a protein.

the precise order of the four nucleic acid bases, also known as sequencing, was done under the Human Genome Project. Its goal included a complete catalogue of every human gene, assisted by computers (Fig. 6.4). Work on sequencing the genome is almost over (Box 10).

For the first time, the ability of the biological molecules to selectively bind with other molecules can be combined with the ability of nanoelectronics to detect the slightest electrical change caused by molecular binding. At a length of two metres and a width of two billionths of a metre, the genome is a big library but on a nanoscale.

In view of their size relative to biological samples, carbon nanotubes have emerged as excellent devices for molecular sensing and manipulation (Fig. 6.5). Carbon nanotubes can provide very accurate lateral resolution of

samples and probe deep features without being affected by the water in tissues. They are, however, sensitive to ambient conditions such as the presence of molecular oxygen. Already, some nanotube probes have given insights into nerve degeneration in Alzheimer's disease.

Both single- and multi-walled nanotubes have been widely used as tips attached to scanning electron microscopes. The high conductivity of the nanotube allows undistorted flow of electrons from inside the samples in microscopes and provides an image of the sample. While atomic force microscopy provides images of the structure and dynamics of individual biological systems, their chemical behaviour needs to be studied as well.

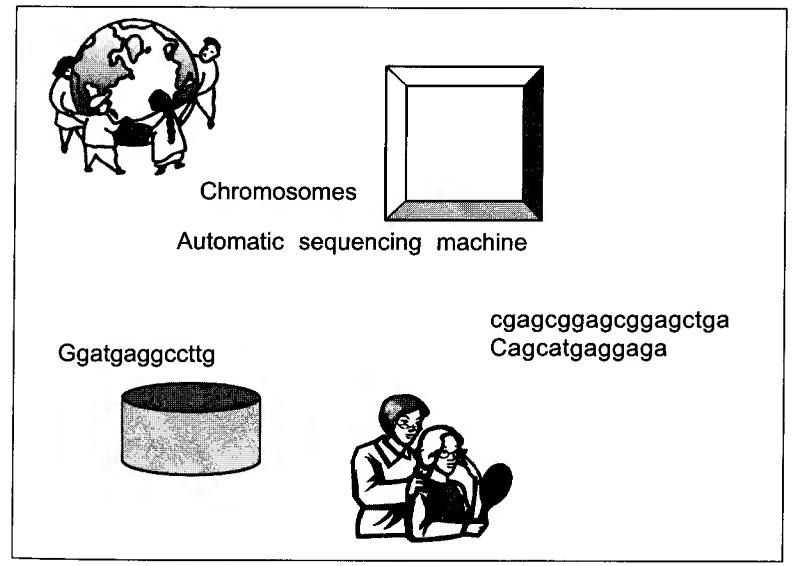


Fig. 6.4: Spelling out the human genome by computers. DNA from a variety of people is shredded into short segments and fed into an automatic sequence machine that reads each genetic letter and puts them together. The computer is instructed to detect the start and the end letters of a gene. Once the reading (sequencing) is complete, the genes are identified. It is a further challenge to discover which genes make proteins that may cause disease or safeguard one's health.

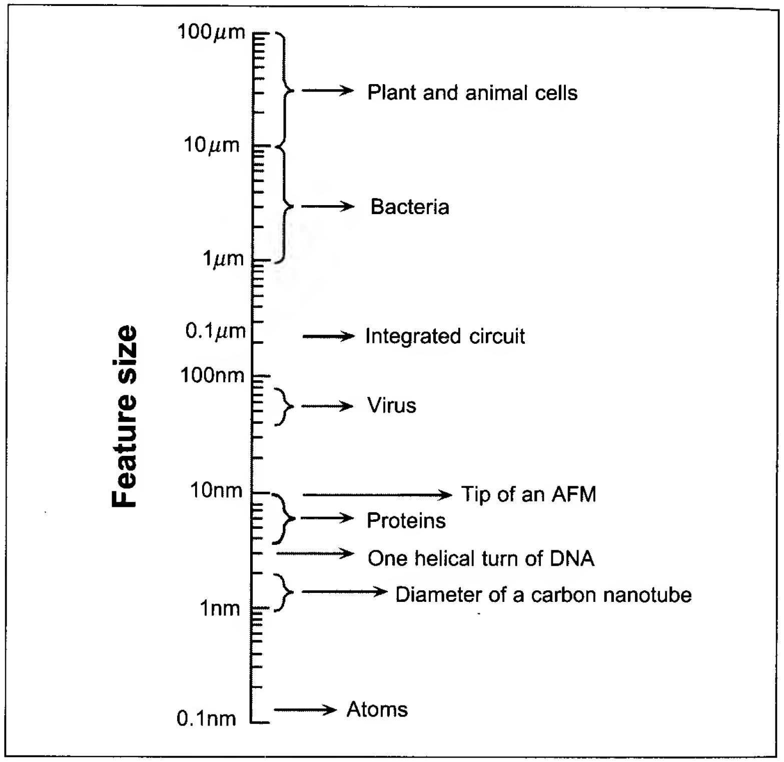


Fig. 6.5: The size and scale of biological samples and carbon nanotubes: A comparison

Most biosensors based on nanoparticles are in the mesoscale (10–100 nm) or in the macro scale (more than 100 nm) with fluorescence as the detection method. The sensors are capable of measuring calcium, sodium, potassium, oxygen, glucose as well as biological warfare agents (such as anthrax). Biosensors may work singly or in parallel with millions or billions of individual units. A sensor may function as a lab-in-a-chip and detect even a single molecule. Or several sensors may work as an array. Microarrays will revolutionise the study of the functioning of the genes and proteins and are expected to provide new insights into the

Box 10

The Human Genome

The Human Genome Project, a worldwide research effort, determined the sequence of the complex chemical, deoxyribonucleic acid (DNA). Known as the 'book of life', the genome was deciphered in 2000. Teams in the US, Britain and Europe as well as the private Celera Genomics Corporation figured out the three-billion-letter alphabets that determine our existence. It is a blueprint for an individual. It will fill 750,000 pages when typed, single-spaced, on A-4 paper. The work of determining the sequencing the code was virtually completed in April 2003.

The human genome is provided in 46 packets called chromosomes—23 inherited from the mother and 23 from the father—or carriers of our genes. This double stranded module is a sequence of nucleotides. The genetic message is spelled out in four bases, viz., adenine (A), cytosine (C), guanine (G) and thymine (T), grouped into threes. A pairs with T and G with C to form rungs of a ladder. This quartet of molecules is nearly identical differing chemically by only a few atoms. A typical gene contains several thousand bases. Each gene is a single instruction for the make-up of a being. This is Nature's encyclopaedia of information. Until recently, it was thought that a human has about 100,000 genes. Latest estimates have reduced the figure to about 30–40 thousand only.

Sequencing or DNA decoding is the process that determines the precise order of the four nucleic acid bases—A, T, G and C that comprise the DNA of all living cells. The genome consists of about one billion base pairs.

Chromosomes come in pairs; one of each pair is inherited from the mother and the other from the father. Though each parent contributes half of his or her genome to the child, essentially a stranger emerges! Each chromosome is a chimera of the corresponding chromosomes in one of his or her parents. When sex cells are forming (eggs and sperm) the individual members of the 23 pairs come together and swap. The 'daughter' chromosomes are separated to become 23. Where

the copies of the chromosomes do not contain the same chemical letters, the gene can lead to disease. These variations on a given chromosome have been the focus of considerable research.

The sequence code is posted on the Internet for all to see and study. The essential step has been taken to unravel the secrets of the genes. They are still hidden in a code of four letters, strung over 23 chromosomes. Most genes encode sequences of amino acids that make up proteins.

If one imagines a chromosome as 1,000 km long, then a gene is 200 m long with a coding region of 10 m; a nucleotide is just 1 cm long.

Nanotechnology is ideally suited to explore this field. It will enable researchers to know more about the genetic code and its role, as nano devices hold the promise of detecting and treating several inherited diseases even before their outward symbols become visible. The world of biology is being discovered on a nanometre scale.

working of protein sequence or expression of genes. The work calls for more sensitive labelling and detection techniques. The development of the new tools would call for more knowledge on fundamentals such as the behaviour of gases and liquids at or within biological nano systems. Besides detection, nanotube tips can be used to modify or fabricate structures at the molecular level.

Nanobiosensors are analytical devices that carry a biological element such as an enzyme or antibody as well as a transducer, which is but a device to convert the data from the samples into signals for detection. Platinum, gold or carbon are used as transducer materials. The transducer may be an optical, magnetic or electromechanical device. Nanosensors would transform the nature of diagnostics. In the long term, nano devices will change the mode of drug delivery. They would bring about more focused therapy in place of the current hit-or-miss drug delivery. As the targeted cell alone would directly get the drug, side-effects on

healthy cells would be avoided. It would be possible to detect at an early stage the process that enables the tumour to get the body's blood supply. Coating nanoparticles with antibodies and agents that would enhance the magnetic resonance imaging would help detect cancers earlier. Heart attacks and strokes can also be predicted, as the plaques in blood vessels can be detected in advance.

Nanodevices are also being developed to act as detectives of diseases in the DNA. A few examples would indicate the trend. Biosensors to measure blood glucose are under development. A single carbon nanotube can detect glucose. The sensors use gold nanoparticles. Glucose oxidising enzymes are attached to the electrodes in the sensors. When the enzyme oxidises glucose, electrons flow through the nanoparticles to the electrodes, triggering an electric current. The level of the current varies with that of the glucose present. The gold particles provide a pathway.

In another experiment, gold particles were attached to certain target molecules to probe DNA. If a disease is found in the DNA sample, the affected (target) area and the corresponding nanoparticle latch on to each other. Even three or four molecules are enough to distinguish between normal and elevated protein levels. In conventional probes, about a thousand molecules are needed to give off a glow, when biological molecules selectively bind with other molecules. It is envisaged that in the not-too-distant future, one could use the glucose in the blood as fuel cells to power pacemakers or insulin pumps.

Early detection of prostate cancer and early warning of heart attack would become possible with the new nano probes. Efforts are under way to detect specific biological molecules such as those with an affinity for prostate cancer. Such molecules bind to nanowires and trigger a signal.

NASA has developed a hand-held DNA sensor comprising multi-walled nanotubes of 30–50 nm diameter, each

smaller than a red blood cell. The sensor is packed at a density of 100 million to three billion nanotubes per square centimetre. Strands of DNA are attached to the end of the nanotubes. The sensor can also detect proteins, chemicals and pathogens. A comprehensive diagnosis is possible from a drop of blood. The technique would expedite drug discovery by screening millions of different candidates for new drugs and evaluate potential drugs rapidly. Various laboratories in the world are developing detectors to spot specific diseases or genetic disorders.

The door is open to detect and examine single molecules. A team of researchers from the National Centre for Biological Sciences and the Raman Research Institute, Bangalore has constructed optical tweezers to study the mechanics of single molecules and cells. This would enable the scientists to manipulate individual molecules. The optical tweezers work with lasers. Researchers at the Rice University (US) have demonstrated the ability to precisely control the electromagnetic field around nanoparticles. For the first time they have developed a nanosensor for obtaining chemical information of a molecule. The researchers have developed a new type of nano shell for getting data on molecules.

A world record has been established in detecting the smallest mass of a molecule. Researchers have detected 5.5 femtograms or about 5/1000th of a millionth of a millionth of a gram using tiny gold coated silicon cantilevers that are activated by a laser. The vibration of the cantilever is an indication of the mass. Sensors that are 1,000 times more sensitive than are presently in use could soon be made available for detecting single molecules. The cantilever can also be made to absorb DNA particles, proteins or chemical contaminants.

Another new technique developed by them involves a gold-based nanoparticle and a single molecule of sugar.

The two can be bound together and used as a marker to spot specific bacteria seen in fluorescent microscopy. The technique can also reveal the amount of antibodies present in human immune system A biomarker can spot proteins in the blood stream. Its interaction with antibodies could help doctors track optically the protein concentration and evaluate the risk of cardiac problems. A person's genetic predisposition to colon cancer or sexually transmitted disease or cystic fibrosis can be detected by gold particles, each only 1–4 nm in diameter, affixed to a piece of DNA. Nanoparticles are non-toxic, target specific and can be used on live cells.

Tracking Diseased Cells

Semiconductor nanoparticles (known as quantum dots) have been found more effective than conventional methods in tracking diseased cells inside the human body. Techniques have been developed to use nanoparticles to take non-invasive images of plaques—deposits in blood vessels—at a very early stage. The plaques, if untreated, can lead to heart attack or stroke.

A research report presented at the scientific session of the American Heart Association in Chicago (2002) disclosed that scientists used 200 nm-long nanoparticles in magnetic resonance imaging. The particles were loaded with 80,000 atoms of gadolinium (an imaging agent) and molecules that detect a protein found in rapidly growing capillaries. The nanoparticles attach themselves to the protein and their location is revealed by gadolinium. Instead of an imaging agent, a drug can be added to the nanoparticle.

Quantum dots, which were used mainly in the field of electronics in the first decade of their discovery, are emerging as important detective tools for the biologist. One of the features of the dots that had prevented their use in biology is their hydrophobic (water-repelling) nature. Some three years ago, scientists found a way out to make them

hydrophilic (water-loving) so that they can be inserted into the watery cells. What is more, the scientists found that it was no longer necessary to inject quantum dots into cells and that dots could be attached to antibodies that are related to specific problems. Water-soluble dots have been used in an experiment to follow the development of a tadpole in the African claw-toed frog. Its growth was visible after its eggs were fertilised until it developed into a tadpole.

Internal components of cells can be tracked and imaged. Quantum dots are used to label different proteins in living cells and show them in different colours. The dots (e.g. cadmium selenide with a coating of zinc sulfide) can detect cancer cells and can function as breast cancer markers. Recent research has, however, shown that quantum dots with cadmium selenide, could be toxic, if not broken down inside the body after some time. Further research is going on.

The ability to track cells as they differentiate would be a great advantage in stem cell research. Stem cells are considered suitable for regenerating the cells of any part of the body. Dendrimers might be used to track stem cells after their transplant. Medical researchers have conducted experiments on rat brains to find out whether stem cells have indeed made new tissues.

Researchers in Taiwan have reported that they developed an effective tool for biomedical diagnostic testing. Fluorescent markers made from semiconductors only five nanometers long were found useful in detecting specific molecules in tumour cells. Elsewhere, scientists have used quantum dots to get extremely detailed pictures of the inner walls of tiny blood vessels. By injecting quantum dots and then shining a laser beam on the skin of a mouse, the researchers found that the low energy photons were absorbed into the tissue and the dots shone. That was 3,000 times brighter than the conventional dyers. The technique resulted in ultra-high resolution of a living tissue. However,

the toxicity of the dots must be reduced before they are used in humans. The dots may contain cadmium, a poisonous metal.

Nanowires have made it possible to track life within a cell in real time. A nanowire coated with an antibody binds to a target protein, which changes the electrical conductivity of the nanowire. Carbon nanotubes and nanowires have been used to detect specific DNA sequences and proteins. One thousand nanowire detectors, each with a different antibody, can be put into a few square micrometres—the area of a single cell. One can study the working of the cell without destroying them. Researchers control the activity of proteins and DNA using gold nanoparticles. Only a nanotube can study the fleeting processes in the cell. In fact, nanotubes, it is hoped, would reveal much new information.

A Japanese research team has used a chaperone protein to carry and protect quantum dots, preventing them from losing their sensitivity. The selected protein has a cavity to hold the nanoparticle in a stable condition and keep off its toxicity. The dot serves as a label for imaging the tissue without scatter.

A major challenge lies in finding ways of detecting cancerous tumours when they are only a few cells. Nanowire-based sensors could be useful for sensing single molecules and detecting cancer marker proteins. The human cell membrane is only 7–10 nm thick. It functions like a gatekeeper who checks and allows thousands of people a second. In addition, the cell membrane permits other molecules to exit. Drugs or DNA must penetrate the cell's outer wall to find their way in.

Nature has several biomotors such as sperm. In order to understand how they work, scientists of Boston College in Massachusetts, USA have built a molecular motor with just 78 atoms. It is shaped like a wheel and it gets energy

from a molecule called adenosine triphosphate (ATP), which accumulates energy in the cell. Japanese and Dutch scientists have also created molecular motors, though they are not powered by ATP.

In a related development, scientists of McGill University, Canada, have tracked how nanocontainers distribute themselves inside a cell. The containers may carry drugs that can, for example, silence the immuno-suppressants in case of transplants of pancreatic tissue and restore any hormonal imbalance.

A professor of physics, Paul Selvin, at the University of Illinois at Urbana-Champaign, and his team have developed an extremely accurate imaging technique for looking inside the cell and have found a strange phenomenon. Molecules of myosin, that convert chemical energy into mechanical energy, act as a cargo van within the cell.

New Features of DNA

Nanobiotechnology can detect new features in DNA. No longer is DNA considered a static, three-dimensional molecule. It is dynamic and in fact gyrating inside the cell's nucleus. The molecule's movements seem as important as its sequence in the critical decision that switches genes on or off. It is indeed the fourth dimension, viz. time, being added to the description of the molecule.

What is astonishing is the finding that the movements of DNA are indeed connected to the activation of the immune system. It was found, for example, that the immune system gets switched on only if the gene swirls in a left-handed orientation, unlike the right-handed coil described by Watson and Crick. Perhaps the position of active genes in a single cell plays a crucial role in the onset of disease. Perhaps movements of genes may also silence their activity at times. These are some of the new puzzles nanotechnology is set to solve in the next 50 years of DNA application.

Nanotechnologists and materials scientists have begun exploiting the chemical properties of DNA in non-biological fields. Several other features of DNA favour this process, viz. its nanoscale (diameter of about 2 nm), its helical structure and stiffness. Objects attached to DNA can be positioned very accurately. DNA can work as glue as well and that too as an intelligent one, as it would recognise and lock with the complementary base sequences. Researchers have found DNA a good building material. DNA can also be a fuel adequate to power a nanoscale device, as when complementary strands of DNA combine, the base pair releases energy. Researchers have found the molecule's extraordinary precision and recognition capability useful in assembling new materials or bringing about the self-assembly of molecules.

Scientists have started constructing DNA arrays and nanodevices to use DNA as scaffolding for assembling other molecules: biological macromolecules as well as electronic compounds are integrated in nanoarrays. Today, DNA is considered a potential source of basic material for nanoscale engineering. DNA is viewed as an ideal building block to make nanometre scale structures. An in-depth understanding of the structure and function of DNA may give researchers new ideas for developing innovations. For example, synthetic molecules may be made to carry encoded information, though Nature cannot be imitated fully.

The discovery of the digital nature of the DNA and its complementarity has yielded a new view of biology. DNA is seen as an information science. Scientists can build their own DNA sequences and write new messages into the molecules. The DNA molecules can be used for controlled and reversible assembly of nanoparticles. In fact, the use of DNA for this purpose has been demonstrated in the preparation of cadmium sulphate nanoparticles.

Italian scientists have studied electrical transport

properties of DNA. They chose guanosine as it self-assembled into an ordered structure. The DNA base was used for building an electronic device. The scientists made a field-effect transistor. They claimed that they had derived higher voltage than from other molecular devices.

Understanding Proteins

Now that the Human Genome Project is almost complete, scientists are taking on the next major challenge of deciphering the proteins. Proteins are the brick and mortar of cells. They are large molecules composed of amino acids that perform most life functions. All cells have essentially the same genome. However, they differ in having different active genes that make proteins. A typical cell makes hundreds or thousands of proteins.

Genes provide only the recipes for making the proteins. It is now known that one gene does not provide for just one protein only. In fact, a gene can instruct several proteins and one protein can have many functions. New disease-markers and target areas for drugs are expected to be identified following a better understanding of proteins.

More significantly, genes do not work alone. They hobnob with one another, forming a co-operative network. Atomic force microscopes (AFM) would be useful in understanding the protein-folding mechanism—a key question in structural biology for the last three decades. Folding takes place in a few thousandths of a second.

Proteins, typically 1–10 nm long, are studied in a process known as nucleation. The unique diffraction pattern of a protein is obtained by subjecting it to X-rays after crystallising it. In this process, molecules come together and separate. Experiments are done on single molecules and the results compared with computer simulations of protein behaviour. The effort would be useful in understanding protein misfolding, which leads to various diseases.

Researchers would be able to acquire the capability to manipulate and interfere with single molecules. Improved Raman spectroscopes would be useful in gaining new insights into protein function in certain common diseases. Since the 1980s, short-lived phenomena appearing on a nanoscale such as cell division have been studied.

Tracing a protein is a challenge. AFMs enable scientists to measure changes in the protein positions over time and manipulate and interfere with single molecules. This is significant as scientists are racing to catalogue the proteins. The main issue in folding is how the amino acid sequence of a protein encodes its final structure and function.

Unlike the four DNA bases, proteins have 20 building blocks, called amino acids. They are the molecular building blocks from which proteins are made. Genes specify which amino acids should be tied together. Direct observation of proteins in buffer solution has become possible. Once identified, the protein structure is logged on to a program in a computer. Powerful computers are required to figure out the order of the amino acids and the protein's shape. Though the task looks simple, it is estimated to involve a mind-boggling number of calculations every second.

Currently the objective is to decipher the structure and function of all proteins made by the human body. Nanowires can detect thousands of proteins secreted by a cell. Nanosized fibre optics with gold particles can be used to turn specific proteins on and off. Nanowires coated with an antibody can bind to a target protein. The protein changes the nanowire's conductivity, which is measured by a detector. Carbon nanotubes and nanowires are used to detect specific DNA sequences and proteins. In an experiment, 1,000 nanowires were jammed into the area of a cell. Such experiments would be useful in tracking the life within a cell in real time. Hand-held sensors could be developed for molecular diagnosis.

An international alliance of industry, academicians and government institutions has initiated the Human Proteome Organisation for this purpose. The task is not easy, because unlike the genome, which is static, the proteome (the set of all proteins expressed) changes in response to internal and external influences. There are ten times as many proteins as are genes. A major challenge is to find out how a two-dimensional line or sequence of amino acids would fold up into a three-dimensional protein.

A Long Way To Go

In spite of remarkable breakthroughs, it is not correct to assume that we now understand how the genome is expressed and how a cell functions. We are far from knowing how the collection of bases leads to a working cell. We have to figure out the proteins that the genes encode and what they do, how do they do the job and how proteins collaborate to carry out the processes in the cells.

One of the biggest challenges is to understand the arrangement of control proteins on the DNA within a cell. It is a natural wonder how a five-micrometre diameter nucleus can package a meter of DNA. The packaging of DNA within a chromosome is nanotechnology at its best!

Even in the late 1970s, it was discovered that long stretches of apparently useless or junk DNA (forming about 96 per cent of the human genome) are sandwiched between genes. Until recently, non-coding DNA was viewed as useless. But recently many surprises have sprung up.

The so-called junk DNA seems to be highly conserved over millions of years of evolution in both humans and mice. Both species, it is now discovered, have hundreds of non-coding areas, as revealed by the mouse genome sequence. The non-coding areas do seem to have a key role, perhaps in pairing the chromosomes before cell division. The sequences that do not code for proteins may in fact control other genes in ways that are yet to be understood. Perhaps they are sign-posts to indicate the location of genetic differences.

The human genome contains 234 'gene-poor' sections ranging in length from 620,000 to 4,000,000 bases. And 30–50 per cent of the estimated genes (40,000) seem to have no function at all! Scientists are interested in picking out the DNA involved in gene expression. Not all of the genes are expressed in a tissue and less than 10 per cent of the DNA is used to make genes. Hence researchers examine when, where and under what conditions genes are expressed. Some researchers use X-ray crystallography to view the 3-D structures of proteins and find out their function.

Scientists have found a powerful way of shutting down or silencing genes by using ribonucleic acid (RNA), which like DNA consists of strings of chemicals. Until about six years ago, it was thought that the RNA simply carries out the DNA's instructions. It is now reported that the RNA can be used even to silence specific genes.

In a recent development, scientists at the University of Chicago have engineered proteins to form the core of gold nanoparticle instead of DNA, as the DNA strands tend to break down easily. The scientists used yeast prions, which are related to some harmful proteins, to form stable fibrils (tiny fibres). Scientists at the Cambridge University (UK) are also using protein fibrils to build electronic materials. Researchers have developed proteins that can bind to some 30 different electronic and optical materials and assemble them into structures.

It appears that it is the genetic activity and not just the number of genes that seems to make a big difference between a human and an animal. The genetic similarity between humans and chimpanzees is striking; it is estimated at 98.7 per cent. Still, humans are vastly different from them. The reason seems to be genetic activity in the human brain, which has evolved 5.5 times faster than it did in the chimps.

And so the mystery deepens, calling for nanoprobes to unravel them.

As it is now possible to change the sequence of the DNA, customised genes may be made to produce customised proteins in turn. And proteins are going to be significant tools for creating nanostructures.

7

SPELLLING MISTAKES AND DEVILS

Life is a mystery. Amazingly, it hinges on incredibly small things.

—A Report

It is a happy coincidence that the right tools for exploring the nano world within us have emerged at the right time, when the 'Book of Life' (the genome) has opened. Progress in the use of innovative microscopes and advanced fabrication technologies enable scientists today to probe and even manipulate biological structures. The minimum feature in today's integrated circuits is smaller than cells and bacteria.

An important discovery explains why every individual is unique. Most of the variations between any two individuals are now traced to differences in the genetic code. The variations in DNA sequence or small genetic mutations may result from just one single chemical letter change. Called single-nucleotide polymorphism (or SNPs—pronounced SNIPs), these are areas where the DNA sequence varies from person to person by a single genetic letter or a nucleotide. These changes in the single base pairs occur at millions of sites in the genome. They may affect gene functions depending on their location and exact base change. They play a role in making each one of us unique. If a SNP is inherited with a disease, it may indicate the presence of a gene that is prone to the disease.

Although 99.9 per cent of one's genes are identical to

anyone else's, the 0.1 per cent difference between any two individuals would account for about three million differences! These 'spelling mistakes' in the genes are harmless most of the time but at times serve as signposts indicating disease or susceptibility to diseases such as diabetes, heart problems and cancer. Groups of SNPs acting as markers for blocks of DNA and combinations of the blocks, called haplotypes, seem to be linked to particular diseases. The spelling mistakes are seen on average once every few hundred nucleotides (about 1,300 bases). The differences also explain why the same drug does not work effectively for all and why some are more prone to a disease than others. Specific SNPs are associated with different medical conditions. It is ironic that the so-called 'minor' variations in DNA are at the root of major differences among people.

Though genetic variation is essential for evolution, SNPs may cause trouble. Many variations disrupt the gene function directly. For example, cystic fibrosis or muscular dystrophy is caused by mutations in single genes. Over 100 such monogenic variations have been identified. In contrast, some variations act indirectly, by encoding for example an enzyme that predisposes people to heart diseases. SNPs in a gene called LPL, which encodes an enzyme involved in fat metabolism, predispose individuals to heart diseases.

The Devil in Details

A major discovery in the detailed analysis of chromosomes is the genetic marker indicating specific diseases. The devil, as the saying goes, is in the details. A genetic marker was found in 1983, long before the human genome was fully documented. The marker was tucked away in chromosome-4, accounting for Huntington's disease, a devastating neurological disease. It was traced to a specific mutation of a single gene, called monogenic disorder. Subsequently, polygenic disorders including coronary heart problems and most

forms of cancer, in which genes act in conjunction with environmental and behavioural factors, have been detected. A mistake at codon 403 (a sequential triplet of DNA, which will add a wrong amino acid in a long chain of amino acids) was found to cause fatal heart disease. Genes associated with breast cancer were also identified. Those, who have variations in the enzyme cytochrome P450, do not convert the painkiller codeine into morphine. The link between disease and the mutated form of gene in specific locations on chromosomes was established. Future diagnostics and medicine would be based on the findings of the specific genes involved.

In 1982, the first genetically engineered insulin became commercially available. A new technique (called polymerase chain reaction) was developed which would become a major means of copying genes and gene fragments. The genes causing more than 1,000 human diseases were soon located. In 1989, the gene connected to cystic fibrosis was identified. The first gene that indicated the possibility of breast cancer (BRCA1) was discovered in 1994. Next year a gene associated with Parkinson's disease was located. Nanotechnology seems to have arrived in time to refine the search and findings.

Signs of genetic defects could be detected even before birth. It was found that around the eighth week of pregnancy, a mother's blood would contain cells from the developing foetus. Analysis of the blood samples would reveal genetic defects, if any, and obviate the need for invasive probes.

The search has begun to understand the genes in maintaining the body's functions as well as the effect of any abnormality. The discoveries made already are truly fascinating. Nanotechnology offers the means to identify and refine our understanding of the genes in chromosomes and their role in diagnosing the possibility of many diseases of genetic origin (Box 11).

Box 11

Some Hidden Devils

Here are a few recent findings of the links between certain diseases as well as benign functions and the genes located in some of the chromosomes. (The numbering of chromosomes is arbitrary.)

Chromosomes 2 and 12	Genes that may cause loss of memory, and late onset of diabetes
Chromosome 3	Gene that may cause lung cancer.
Chromosome 6	Wrongly described as the seat of intelligence; not all intelligence is genetic.
Chromosome 7	Genes account for the innate instinct for 'grammar' displayed by children in speaking (any language); also involved in cystic fibrosis (diseases of the lungs and intestines) and obesity.
Chromosome 8	DNA fingerprinting (means of determining parenthood, tracing criminals etc.).
Chromosome 9	Has a gene that makes an enzyme, which converts cholesterol into cortisol that suppresses the immune system.
Chromosome 10	Involved in maintaining the sensitivity of ears, nose, eyes; it also enhances stress.
Chromosome 11	A gene that has a recipe to make a protein called dopamine receptor, which controls the blood flow through the brain.
Chromosome 12	Genes that control the development of body parts into the required shape.
Chromosome 13	Gene that may cause breast cancer.
Chromosome 14	Alzheimer's disease (loss of memory, generally in old age).
Chromosome 16	Genes for learning and memory.
Chromosome 17	A gene (TP53), considered to be the 'guardian angel of the genome', as it suppresses tumours; if it is broken, then chemotherapy will not work in fighting cancer.
Chromosome 19	A damaged gene leads to coronary heart disease and Alzheimer's disease.
Chromosome 20	Misfolding of just one molecule in a gene leads to the mad cow disease.
Chromosome 21	Smallest human chromosome, which, if damaged, will cause Down's Syndrome (mental retardation and other abnormalities in the offspring).

The findings given above are by no means final or complete. For example, the sequencing of chromosome 20 has already expedited the search for genes involved in diabetes, leukaemia and childhood eczema.

Nanosensors would one day reveal the genetic map of individuals. A more realistic diagnosis would then become possible. Perhaps in the not too distant future, we would wear a silicon chip as a very personal ID indicating the most suitable gene therapy recommended to each one of us by the world's best experts! We may then have the last laugh at the devils inside!

Thanks to nanotechnology, the door is now open to search the roots of many diseases. It will soon be possible to scan the DNA for genetic diseases. In one method, fragments of DNA can be affixed to nanoscale gold particles on a microchip. The DNA will recognise targets (genetic material showing diseases or disposition to diseases), which will stick to gold particles. Several sensing elements can be attached to a chip. Besides finding the DNA that is targeted, it would be possible to catch any one segment of DNA and read its genes. The DNA on the microchip could be fluorescently labelled and an optical detector could 'read' the specific sequence of the genetic content. Millions of DNA-labelled channels may be used.

In another technique, gold particles may be attached to a piece of DNA and exposed to magnetic field. When the particles heat up, the DNA breaks up into two strands and

rejoins when the magnetic field is withdrawn. This technique could be further developed to provide the ability to switch genes on and off.

Several private companies have taken up projects to discover drugs based on SNPs. A company in Iceland (called deCODE) has involved much of the country's population in its research. Iceland is ideally suited for such work because it has excellent genealogical records of its people, making it easy to track SNPs down the generations. Moreover, the people are quite cooperative and they donate DNA for comparison with the diseased genes. The firm has found (2003) the general location of genes connected to 25 diseases caused by genetic abnormalities and pinpointed the genes for seven such diseases.

Over a million SNPs have been catalogued in the human genome. Thousands of them change the amino acid sequence of proteins. Our genetic predisposition to colon cancer or sexually transmitted disease or cystic fibrosis can be detected by gold particles—each only 1–4 nm in diameter—affixed to a piece of DNA.

A database from the University of Tokyo simplifies the job of locating medically important SNPs. It is believed that an individual has about three million SNPs; of this the first 'map' of about 800,000 SNPs has been published. Recently, researchers have mapped about 1,83,000 SNPs in chromosome 6. It is the largest chromosome sequenced so far (as of November, 2003) with a staggering number of base pairs totalling 166,880,988.

The world's largest medical charity, the Wellcome Trust and ten major drug companies have in a joint project started to map all the SNPs. Many SNPs are publicly available (www. ncbi.nlm.nih.gov/SNP). The International Hap Map Project was formed in 2002 to describe the patterns of genetic variation. A Hap Map is expected to serve as an index to the 'Book of Life' (the genome). It will help researchers

rapidly search for SNPs to identify blocks of common sequences of DNA (or haplotypes as they are known). The genetic data for the samples required in the work will be gathered from different populations in many continents of the world.

Biotechnology companies have patented some of the SNP technologies. A recent survey showed a sharp increase in the number of scientific papers and patents since 1987. There is a growing demand that the data on SNPs should be available without any restriction on grounds of intellectual property rights. Accordingly, a public-private consortium has placed about 1.8 million SNPs in the public domain (as on January 2003). Ultimately, prediction of disease risk and response to therapies could be made available to individuals. Detecting mismatches between base pairs in DNA would soon be possible with a hand-held DNA sensor.

A Drop-out Succeeds!

A young drop-out from Harvard Medical School, Eugene Chan, prepared an innovative technique to rapidly read the variations in an individual DNA. He developed a device that was programmed to detect only the variations in the code and ignore the unchanging part of the DNA. A detector, based on his idea, could spot variations on DNA segments of 200,000 bases. Chang hopes to expand the readout capacity severalfold.

Though the history of immune therapy dates back to Jenner's introduction of a vaccine (1796) to prevent recurrence of smallpox infection, significant progress in this field was made only after the genetic origin of diseases was detected. A year after the DNA model was discovered, Jonas Salk and Albert Sabin introduced (1954) live (attenuated) as well as dead polio vaccines. It made a big difference in the fight against poliomyelitis.

The Importance of Being a Mouse

The effort to track down the origin of several diseases to genetic variations has emerged at an appropriate time in the history of drug discovery. It is only in the last three decades that the fight against some of the dreaded diseases has begun at the molecular level. Nanotechnology would provide sophisticated weapons to win the fight, which is essentially based on giving a chance to the immune system to work without fail. The role of nanotechnology in this field can be better appreciated in the light of some of the path-breaking discoveries based on strengthening the body's defence mechanism.

The body's antibodies and 'T Cells' spot all abnormal protein fragments, called antigens, produced by diseased cells. Specially engineered versions of the body's own antibodies (which bind to specific substances, usually proteins) can track down specific cells and destroy them without many toxic side effects.

By injecting mice with infectious antigen (which is recognised by the immune system as foreign and dangerous to its well-being), scientists stimulated the production of antibodies against the disease in the mice. But the effects were not quite effective. As mouse-derived antibodies provoked adverse reactions in patients, the search was on for developing a different type of antibody. In 1975, Georges J.F. Kohler and Cesar Milstein of the UK Medical Research Council's Laboratory of Molecular Biology in Cambridge devised an innovative procedure for monoclonal antibody generation. The technique was useful in mass production of what is known as monoclonal antibodies (Fig. 7.1).

The technique involves injecting mice with an antigen to get antibodies from them, isolate the antibody-producing cells and fuse them with immortal B-lymphocytes from the human bone marrow. The resulting hybrid cells (hybridomas) are then mass-produced as monoclonal

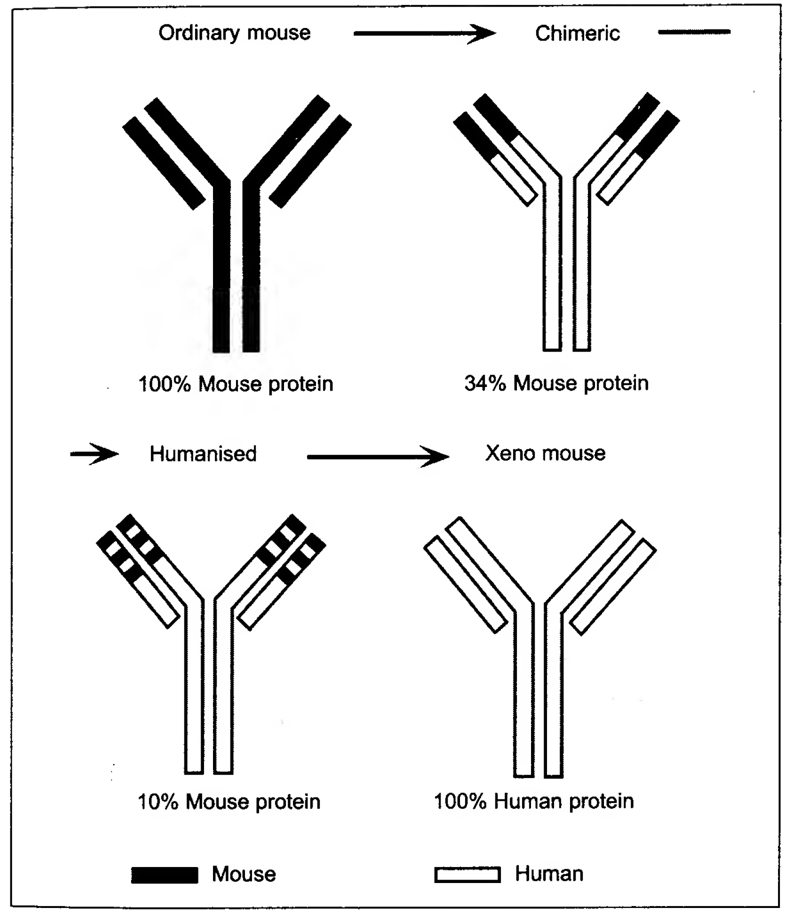


Fig. 7.1: Evolution of antibody technologies. The basic monoclonal antibody (that recognises harmful substances) is schematically shown as a large Y-shaped molecule. In the early experiments, when an antigen (a substance which the immune system of the body recognises as foreign or harmful) was injected into a mouse, it induced the animal to produce antibodies to fight the antigen, but with 34 per cent or 10 per cent mouse protein sequences. Hence the body rejected them. Only antibodies with 100 per cent human protein sequences were found effective in humans. Hence the antibody expression of the genetically engineered mice was suppressed and replaced with human antibody gene expression. Such mice could be produced indefinitely and thus made to generate human antibodies to fight human antigens.

antibodies. Milstein and Kohler were given the Nobel Prize for their path-breaking discovery. This process was further improved with another breakthrough in 1986, when mouse monoclonals were 'humanised' (using human proteins) so as to evade the innate tendency of the immune system to reject foreign matter (Box 12).

Several monoclonal antibodies were created. For instance, the US biotech firm, Genentech, has in addition to oncology, undertaken several projects for developing potential therapies for asthma, seasonal allergic rhinitis, psoriasis, organ transplant rejection and inflammatory bowel disease.

Antibodies detect cancerous proteins spread out on the cells, but destroy only about 15 per cent of the unwanted cells. Hence new drugs were developed. Unlike antibodies, T-cells detect even fragments of abnormal protein fragments. The new drugs are called monoclonal T-cell receptors and can detect and destroy all diseased cells.

Experiments have found that magnetic nanoparticles, coated with antibodies to a specific virus such as HIV, could be injected into the bloodstream to detect precisely the location of viruses. In case live viruses are found, they would stick to the antibodies inserted on the nanoparticles. This could be detected in conventional body scanners (Fig. 7.2). Particles with a core of iron oxide have been found to be safe in the body, though further research is on. It has been found that thin films made from semiconductor nanoparticles could have medical applications without any toxic effect, provided they have been coated with the biological material called collagen, a protein found in animal connective tissue.

Northwest University researchers have used gold nanoparticles coated with silver for detecting DNA with unique features that would indicate the presence of specified viruses. Different strands of DNA that would recognise

Box 12

Where Mouse is 'Self'

Specialised cells (called B-cells and T-cells) in the human immune system protect our body against infections. B-cells produce protein molecules known as antibodies, which can recognise potentially harmful substances known as antigens and neutralise them. Antibodies bind tightly to one specific antigen without harming normal cells.

Antibodies are Y-shaped proteins, consisting of a constant and a variable region that is unique to each antibody. The body generates numerous antibodies that can recognise multiple, specific antigen structures. At least 11 antibody products have been approved officially in the US to treat cancer and autoimmune diseases.

The human body, however, quickly eliminated antigens that contained mouse protein sequences. In order to overcome this problem, improved forms of mouse antibodies called 'chimeric' and 'humanised' antibodies were assembled from portions of mouse and human antibody fragments. Still, the body rejected them after a while. Hence, antibody products with 100 per cent human protein sequences were developed.

Researchers are now able to inject rodents with the antigen they want and let the animals give out completely human antibodies. For this purpose, genetically engineered mice are used. The technique consists of suppression of antibody expression in such mice and its replacement with human antibody gene expression. Such mice are bred indefinitely. They generate human antibodies to human antigens and hence the body recognises the antibodies as 'self'.

Researchers think it would be possible to use dendrimers, highly branched synthetic polymer for preventing immune response in the transplant of animal organs. Dendrimers, by virtue of their shape, can capture small molecules in the cavities.

Known as Xeno Max technology, samples upto two million B-cells per immunised Xeno Mouse animal are taken to choose optimal therapeutic products. Clinical trials have begun, though

it is not certain that the technology will generate antibodies against every antigen to which they are exposed.

At least 400 other monoclonal antibodies were in clinical trial in the world (as of 2002). A survey by the Pharmaceutical Research and Manufacturers of America showed that antibodies accounted for over 20 per cent of all biopharmaceutical products in clinical development.

different targets in the DNA and attach themselves to them are inserted on a chip with dye molecules. Using a Raman spectrometer, the researchers have been able to detect the dye molecules corresponding to the target DNA and the disease.

German scientists have developed sensors with nanoparticles that are designed to spy on the binding of molecules. The sensor detects and measures the light scattered by the nanoparticle as a result of its contact with the molecule. The sensor has potential use in detecting the binding of an antibody with an antigen.

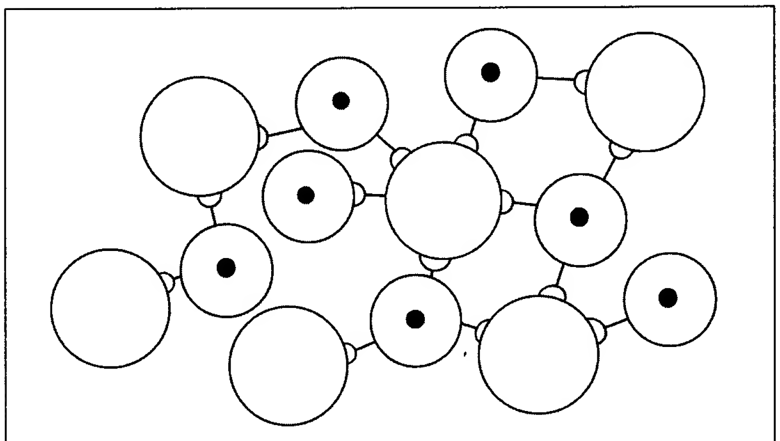


Fig. 7.2: Magnetic nanoparticles with antibodies (shown as circles with dots) can bind to viruses (bigger circles) and the resulting cluster is seen in conventional body scanners for medical diagnosis.

An Ultra-thin Gatekeeper

The human cell membrane is only 7–10 nm thick. It functions like a gatekeeper who checks and allows thousands of people a second. In addition, the cell membrane permits other molecules to exit. Drugs or DNA must penetrate the cell's outer wall. When capsules are swallowed, the drugs inside penetrate the membrane of the cells that line the digestive system. However, several antibiotic drugs cannot do so. Some others cannot get out of the blood flow or go through the blood-brain barrier. But cell membranes have 'transporters' that will allow molecules of a specific size or chemical make-up. For example, one such transporter can check out about 10,000 molecules a second. The transporters in a healthy cell look different from those in tumour cells. Drug manufacturers therefore seek such transporters.

The success of gene therapy depends on delivering the desired genes into cells. Basically, scientists try to understand how DNA is transported into cells, structured as they are with lipids. Effective gene therapy requires that the corresponding DNA be condensed into small particles of say 50–100 nm so that they can get into cells. It is not enough to package DNA meant for gene therapy into nanometre size particles of selected polymers. It is equally necessary to make the nanoparticles uniform in size and protect them from the cell's destructive power. Several polymers have been made after much trial and error so as to ensure the success of gene therapy.

For a long time, scientists wondered about the mechanism that could pull a strand of DNA into a carbon nanotube. It has been found that the weak force between atoms and molecules (called Van der Waals' force) as well as the hydrophobic force (shy of water) do the work. German scientists at the Max Planck Institute showed on the basis of computer simulations that DNA could be inserted into carbon nanotubes. Researchers at Oak Ridge National

Laboratory and the University of Tennessee have in fact used carbon nanotubes to insert DNA into cells. The technique is described as a step towards genetic modification. Scientists are now confident of using DNA molecules for writing new messages in the genetic code in the future. Researchers at the Indian Institute of Chemical Technology, Hyderabad, have developed synthetic peptide-based nanotubes. The tubes can be used for delivering DNA material for gene therapy and for making biological sensors. Researchers at the Benaras Hindu University (Physics Department) have used DNA template for alignment of silicon and germanium nanoparticles. And chemists at the University of Delhi have developed a magnetically guided drug delivery carrier, encapsulating bioactive compounds. The biodegradable carriers are guided by externally placed electromagnets.

Dendrimers: Wonder Molecules

Drug delivery systems inside the human body depend for their success on the ability of the drug and its carrier to penetrate the human cell membrane. Dendrimer, the Greek word for 'tree', is a synthetic polymer that branches out. Dendrimers have been found useful for this task, as they effectively find their way into cell membranes. They can be used as decoys to prevent viruses from reaching cells. An artificial molecule called organic dendrimer—2–20 nm across—is used for imaging as well as drug delivery. Dendrimers are magnetically tagged and injected into the body. And the iron oxide used in tagging can easily be traced.

Dendrimers, being water-soluble molecules, have strong chemical bonds and can take a drug (e.g. for AIDS) right into the affected cells, what with their tree-like, highly branched appearance. In fact, several roles are envisaged for this molecule: binding to receptor molecules in the affected cells; detecting the shape of the cell or tumour; and release of drugs on demand as programmed without

hitting the healthy cells. Dendrimers can also be useful in the transfer of DNA to cells. When this technique is perfected, gene therapy will become commonplace. Tests on animals have been planned in the first instance. The basic objective is to make drug delivery a precisely targeted method.

In another method, very small beads coated with gold, called nanoshells, are attached to dendrimers. Once inside the body, the nanoshells can be heated from outside by infrared waves and activated. One nanometre-long buckminsterfullerene molecules (soccer-ball shaped molecules made from carbon atoms) can transport dendrimers and release drug dosages, when they encounter certain molecules. Rice University scientists have shown that buckyballs could be used for drug delivery in the case of an anthrax attack. Buckyballs, which seemed to have been eclipsed by carbon nanotubes, are coming into limelight once again; their cost of production has also come down drastically.

Nano Submarines

Nanoscale machines already exist, say the researchers, as functional molecular components of live cells such as molecules of protein or RNA. Fluorescent probes have emerged as ideal tools for real time imaging of live cells. This would enable researchers to record and measure events inside the cell such as biomedical expression and enzyme activation.

A nanoscale 'submarine'—only a few tens or hundreds of atoms long—is made to navigate through blood. They are submarines that flow in your bloodstream. Their target: destruction of a programmed disease. Is it science fiction? Not really. A model has already been simulated on the computer. A prototype is just a couple of years away (Fig. 7.3).

You may wonder what powers it? Surprisingly, it is bacteria including the familiar *E. coli* and salmonella. They are supposed to be the engines that pull and push the

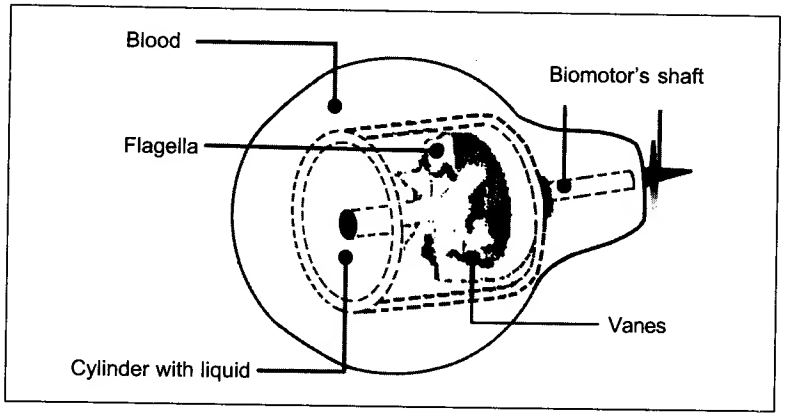


Fig. 7.3: A nano 'submarine' that can navigate the human bloodstream and attack disease. Bacteria such as *E. coli* may be the perfect 'motors' for the submarines that can push or pull a disc with drugs to treat tumours or unblock arteries. In this experiment, scientists have used only the flagella from the bacteria, the size of the biomotors being around 100 nm.

submarine. They carry a tiny cylinder filled with drugs. The drugs are designed to fight tumours, or melt the unwanted fat in the arteries. Nanoparticles can cut blood supply to tumours and can pack a gene for promoting self-destruction of cancer cells. Research is under way to ensure that there are no side-effects.

A new pathway to cell membranes has been attempted. The Scripps Research Institute in California has made its own transporter. The research group used peptide (protein fragments in cells) nanotubes for drug delivery. Peptides can be used as mould for casting silver nanoparticles inside. The peptide is biodegradable and water-soluble. Hence it is safe to transport drugs in them.

These efforts underline the realisation that drugs cannot reach many parts inside the human body. Nanodevices would make drug delivery more effective and less painful. For instance, pancreatic cells are encapsulated into nanoparticles that are sent into the blood stream where they

continue to secrete insulin without being attacked by antibodies. Drugs packaged inside nanoparticles will have no toxicity. A cardiac drug can be taken without the risk of its potential adverse impact on the kidney or liver. Moreover, cancer treatment without side-effects is also possible. The Memorial Sloan Kettering hospital in the US has developed a cancer treatment generator to inject radioactivity in small doses to the affected areas. This avoids side-effects that follow the current practice of blanket treatment. Nanoparticles may help cancer patients in another way too. Currently, photosensitive drugs, when exposed to laser light, destroy cancer cells in tumours. However, patients become extremely sensitive to daylight for up to six weeks. Ceramic-based nanodevices (0.5–1 nm) can be used to carry the drugs and avoid the unpleasant side-effects.

Radiation-damaged cells can be detected thanks to nanosensors. This would be of use to astronauts in space. Nanosensors would be able to reveal the different proteins that surface if the cells are damaged. The drugs carried inside the nanoparticles can either cure the cells or destroy them.

In a cell hit by cancer, its self-regulation programme is silenced, leading to unregulated growth of tumours. The natural programme, called apoptosis, would make such a cell commit suicide. Its silence would let cancer grow. Researchers have developed a gene, which encodes for a protein that can trigger apoptosis in cells, while sparing the normal ones.

In another approach, nanopulses have been found to be effective in changing the structures within cells and in triggering the cell to commit suicide by activating the needed enzymes. This finding has led researchers to examine the role of suitably treated nanoparticles in healing wounds and reducing obesity.

In a significant application, nanoparticles have been used to cut the blood supply lines to tumours. A nanoparticle

is packed with a gene (Raf-1) that forces blood vessel cells to destroy themselves. The beauty of the gene is that it destroys only newly formed blood vessels and not established ones. Moreover, as it is a nanoparticle and not a virus, there is less chance of it being rejected by the human immune system.

Two recent procedures to attack cancer cells incorporate some novel features. Iron nanoparticles and monoclonal antibodies are attached to bioprobes about 40 nm long. Millions of bioprobes are injected into the patient's body. Once inside, the bioprobes sniff out and aggregate near the tumour cells. Magnetic fields are generated from outside and as a result the iron is heated to 170ºC killing the cancer cells.

In another approach, spherical nanoshells of gold and silicon are injected and they pile up near the tumour cells. An infrared laser is used to heat the shell. An advantage of this method is that the probes could target cells too small to catch the surgeon's eye. The patient also does not feel any pain in either of the applications and healthy cells are not affected.

In another application, a firm has discovered a protein that can be used for retarding or reversing osteoarthritis. Nanoscale building blocks can be used to provide a base for growing bone cells. Nanotechnology would be useful for developing superior implants for use in the repair of tissues, skin and cartilage.

Dutch scientists have developed a genetic tool to test whether breast cancer at the very early stage needs aggressive treatment. A similar device can test water supplies for possible anthrax that may be introduced by terrorists.

Chemically reactive organic groups can be attached to nanotubes. Specific nanotubes can be attached to preset location. Nanotechnology makes it possible to trace viruses inside the body (Box 13).

Box 13

When the Ganga Cured

Billions of years of evolution has given viruses some unique features, now been discovered. A virus has an extraordinary capacity to go to specific cells and exploit the host's hospitality.

It is interesting to recall that towards the end of the 19th century, a British chemist, E.H. Hankin found that the water from the River Ganga checked the spread of cholera. But when the water was boiled and taken, it did not cure the disease! Again, in 1915 another researcher identified the agent as a virus, which attacked the disease-carrying bacteria. It is now known that the virus supplied its own DNA and acted as a smart weapon by ultimately killing the bacteria.

In Georgia, in the former Soviet Union, doctors used phages (viruses) from hospital wastes to kill selectively chosen bacteria and cured several diseases. There are no side-effects resulting from the phage injection and it only addresses harmful bacteria. An Indian company (GangaGen) is reported to have kept 400 phages for curing various conditions.

Nanobiotechnology makes it easy to follow the viruses allowed inside the body. Moreover, nanotechnology makes it possible to reconfigure deadly viruses into friendly agents to image diseased cells as well as fight them.

Scientists plan to take advantage of this capacity but for a good purpose. Researchers have plans to first immobilise viruses by denuding them of their infectious cargo (nucleic acid) and then exploit their docking sites that bind to specific cells. The purified viruses can be used to deliver drugs. For example, anti-cancer compounds inserted inside the nanotubes could be carried to tumour cells.

As even disabled viruses are not risk-free, non-viral approach has also been proposed. It consists of encasing DNA in fatty globules. However, globules that are about 100 nm across cannot go through the cell membrane except when the cell divides. Scientists have reportedly developed a way of packing DNA into a much smaller globule—about 25 nm across. This technique is useful for the success of gene therapy.

As drugs become less water soluble, new delivery systems are needed. The Centre for Biological Nanotechnology of the University of Michigan has undertaken research in this field. Using molecular imprinting, drug delivery systems that can recognise where they are needed inside the body are being developed. For example, insulin can be triggered if glucose exceeds a level programmed to reach many parts inside the human body.

Nanocontainers, composed of polymers, may distribute drugs to specific spots within individual cells. Fluorescent labelling is used to track the journey of nano containers. An interesting feature of such devices is their ability to penetrate some parts of the cell that are targets of drug delivery.

Nanofibres are expected to carry genes into cells. Such devices (with a tip of 20–45 nm across) are to be integrated into cells. The method is useful in exploring the impact of a drug upon cells and carry out precisely-controlled genetic modification in a non-heritable way. Japanese researchers have combined bacterial protein with semiconductor nanoparticles that are luminescent for controlled drug delivery. The Japanese have also developed a nanoporous material that opens or closes the exit of the material. Ultraviolet light at 310 nm closes the exit, while the light at 250 nm opens.

Artificial decoy cells have been developed to fight viruses. The synthetic cells are of the same size as ordinary cells. They have the same receptors for docking with the viruses. Currently anti-viral drugs are given after a virus attack. Now it is injected even before the virus has entered the cell as a precautionary measure. In an experiment, the synthetic virus inhibited one type of influenza virus from infected human cells.

The decoys can be deployed throughout the body or in specific areas affected. Just one injection is sufficient, instead

of repeated doses of antibiotics now prescribed. An added advantage is that virus particles will not rest content until all the bacteria are killed. Scientists of the Centre for Biological Technology of Michigan University have done an experiment to test this phenomenon. Mice, which were fed with a bacterium in oysters, survived when given a virus injection.

The development of microelectronics has led to what is familiarly known as lab-on-a-chip. A chip the size of a credit card has micro channels that are narrower than a human hair. They show the constituent elements such as liquids and gases separately.

Nanotechnology is expected to help scientists discover mechanical properties of tissues and cells and how blood vessels respond to increased blood flow and study the biological response to the force applied to cartilage. This would support engineering of new tissues or repair of diseased ones in an effective way.

Genes and Drug Discovery

Nanotechnology will help discover more effective drugs against many diseases. It is interesting to find that the top 100 drugs have targeted only 45 molecules before adopting nanotechnology. It is now known that all the drugs that have been invented to date can be traced to only 500 genes. At least a tenth of the 35,000 genes or so are now considered possible targets for drugs.

It is time that the developing world situated in the tropics gets due attention in the search for new drugs. Of the 1233 drugs approved in the last decade, only 11 were for treating tropical diseases, and of them, half were intended for livestock!

The drug companies point out that it takes on an average 10–15 years for one of them to develop a marketable drug and it costs an R&D expenditure of about

$800 million. It is a challenge to find positive leads to drug discovery. In the expensive highway of drug discovery, wrong turns will cost a fortune! It is hoped that the benefits of nanotechnology would not remain confined to the diseases mostly prevalent in the advanced countries.

The task of tapping the vast potential offered by the human genome for medicine has just begun. Initial results are encouraging. For example, a gene has been found for a protein that would reduce production of glucose in the liver and enhance the utilisation of glucose. A US company (Genentech) has discovered a human protein that stimulates formation of blood and lymph vessels. This protein is involved in the spread of breast and melanoma tumours. Another protein (microstipen) supports patients undergoing chemotherapy and radiation. Yet another human protein, useful in the healing of wounds, has also been found.

Researchers have an ambitious agenda of developing antibodies for proteins made by 30,000 genes. It is also proposed to analyse 5,000 proteins and their instructions. Numerous private companies are now in the race for protein-based drugs, even as more and more medically significant genes are being discovered. Observers wonder whether these efforts would end up as processes and products of private companies beyond the reach of the common people in developing countries.

Ethical and Social Questions

The potential conquest of the devils is not the end of the story. The ethical and social questions raised by the prospect of one's genome being discovered and stored have to be addressed. First of all, will it mean loss of privacy and social dignity? If someone is branded as a possible carrier of a disease, however remote be the possibility, the risk of social stigma will be there. On a more practical note, will the insurers shy away from those billed as potential victims

of a heart attack? Will the employment opportunity be denied to those who are likely to have problems at a later stage? Who would decide that the 'gene card' could be ignored? Will nanotechnology hasten to pronounce a death sentence even without the benefit of doubt being given to the victim? What about human rights and rights to equal opportunity and will they be bulldozed by the so-called scientific truths? These are profoundly disturbing questions for which there are no easy answers.

8

THE NANO AGE: A PREVIEW

The world has changed far more in the last 100 years than in any other century in history. The reason is not political or economic but technologies that flowed directly from advances in basic sciences.

—Stephen Hawking

A lot of hype about the Nano Age has accumulated in the wake of some outstanding discoveries and innovations. Some of the ideas are no doubt pure science fiction. It is easy to downplay the new age as a western luxury but it takes courage to see and seize the opportunity it offers to developing countries to leapfrog to higher levels of progress. A preview of the Nano Age would indicate the nature of the advances, while pointing out the challenges involved in achieving them.

It is but appropriate to begin the preview with the continued achievements of the man who played a key role in revealing the nanoworld and opened the door to actively modify it for the benefit of humankind.

Dr Binnig, who developed the scanning tunnelling microscope (*see* Chapter 2), was fascinated by the nanoworld revealed by his invention. Continuing his work, he scored another success by proving that nanomechanical techniques could be used to increase the data storage capacity of the electronic chip. He demonstrated it in IBM's 'Millipede' project, which raised the data storage density to a trillion (million million) bits per square inch; it is 20 times higher than the densest storage now available. The capacity is equivalent to storing 25 million printed textbook pages on the surface of a postage stamp! The device uses thousands of nano-sharp tips to punch a thin plastic film to represent individual bits. Dr Binnig envisages a 1,000-fold increase, far beyond the terabit achievement.

Improved Microscopes

It is now possible to have a real time hands-on nanostructure manipulator. Called computer-controlled scanning probe microscopy, it enables researchers to enhance the image quality. Nanomanipulators have been developed to operate in scanning and transmission electron microscopes. They provide a virtual telepresence to explore the nanoworld. In addition, optical tweezers have been developed. They would hold and move nanometre structures while researchers study the dynamics of molecules.

Meanwhile, an extension of electron microscopy has also been reported. Called X-ray microscope, it allows the study of crystallisation. Normally, a crystal is grown to study a protein's shape. However, the initial stage of protein-crystal formation has not been well understood. It is necessary to know the exact shape of a protein, as the shape is related to its biological function. Much information about the sample could be known by studying the way X-rays are diffracted by objects. The X-ray microscope can be used to study semiconductors as well.

Even the good old light microscope has gained by the advances in nanotechnology. A nano-fabricated device has been developed to facilitate the use of light microscopes to look at a single biological molecule. Normally, a standard conventional microscope needs at least 1,000 molecules to make them visible, because of the limitations of the wavelength of light. The nano-enhanced microscope would be

used to watch interactions between nucleotides and other molecules tagged for visibility.

Researchers use atomic force microscopes (AFM) for the production of integrated circuits. Though AFM is a major advancement in imaging surfaces, it has some deficiencies—the large cone angle of the tip makes it difficult for imaging narrow areas, and the tip is brittle and so needs frequent replacement. Carbon nanotube (CNT) has emerged as a substitute. Attached to the AFM's tip, the CNT considerably enhances the resolution, besides offering its well-known strength. CNT tips have also been found useful in imaging thin films and biological specimen.

Varied Uses of Carbon Nanotubes

CNTs are increasingly in demand for development of chemical, biological and physical sensors. Carbon nanotubes have significant technological potential. Their applications would include flat-panel TV display, telecommunication components, lithium-ion batteries, extra strong materials, and fuel cells.

German scientists have made a new type of transistor by growing semiconductor nanowires in a polymer stack. The diameter of the transistor is reported to be 100 nm and a hundred million of them could be packaged into one square centimetre. The nanowires are one-dimensional structures with novel electrical and optical properties and can be used as building blocks in devices such as field-effect transistors, sensors and light-emitting diodes. They combine the flexibility of organic materials with the optical properties of semiconductors. At present these structures do not have the necessary mechanical strength. Further development is under way.

Nanoelectronics is a vast area that is likely to have the initial benefit of nanotechnology. Efforts are under way to realise two objectives: use a simple nanostructure

(e.g. nanocrystal, quantum dot, nanotube) for processing electrical, optical and chemical signals; and to assemble nanostructures for various applications such as information storage.

Today's television set resembles a bulky box mainly because of a high 'gun' inside that shoots electrons at the pixels on the phosphor sensor to light it up as signalled. Alternatively, millions of nanotubes could function as 'guns', one for each of the pixels. This would facilitate the building of flat-panel displays in TV sets and computers at half the power needs of today's sets. Nanotubes emit electrons at low voltage while maintaining the required current densities. Realising this goal in commercial production still needs several innovations. Digital, flat-panel TV is likely to be the first consumer application of single-walled carbon nanotubes. It will consume less power and the nanotube will not melt or degrade inside the TV set.

Research is under way to generate microwaves from nanotubes. When successful, it would transform the economics of cell phones, since weak signals from today's phones have to be amplified by base stations. More lithium ions could be stored in batteries. At present, graphite can store only six carbon atoms for every lithium ion.

A firm has made a prototype of a few dozen nanotubes that can act as a memory element, using carbon instead of silicon. The memory is stored in billions of nanotubes; it can read or write a bit in half a nanosecond (ns), as against 10 ns now being taken for the operation. Their ideal is to achieve data density of a trillion bits per square centimetre.

Components on a microchip are carved on layers of doped or undoped silicon using photolithographic printing. It involves optical focusing of the image of a chip pattern onto a thin film called resist on a silicon wafer, followed by chemical etching. However, photolithography is fast approaching its limit. For a given wavelength of light,

only features half its length can be made. The use of extreme ultraviolet or soft X-rays would only add to the growing cost of photolithography. Hence, a new technique has been developed. Called laser-assisted direct impact, the new technique does not need focusing optics or etching and is similar to making compact discs. It was developed by Stephen Chou and his colleagues at Princeton (US). A laser pulse melts the thin top layer of silicon and presses a mask into it. When the mask is removed, an imprint of the design remains in the silicon. The technique can generate features with a resolution of just 10 nm. The costs are expected to be less than that of the conventional technique. If developed further, it is claimed that it could extend Moore's law by another 25 years!

Fibre Optics and Nano Lasers

If nanocrystals are incorporated in polymers (plastics), the former would emit near-IR radiation, a feature useful in fibre optics that are increasingly used in telecommunication. Scientists have created nanowires that emit laser light in blue or ultraviolet. Nanotechnology is used to produce blue light-emitting diodes (LEDs). Smaller than a grain of sand, the LEDs can give very bright light consuming very little current. Nanowires made of zinc oxide can be used as optical fibres and would soon be integrated with optical fibre network for speech and data traffic. In a recent experiment, scientists have found that the inner tubes in a multiwalled nanotube could be made to slide in and out of the outer tube at a fantastic speed of one billion times a second. This gigahertz oscillation frequency may one day be used in fibre optics as optical filters.

Hollow optical fibres used in telecom networks could be made from an unusual source: certain spiders. The fibres could be just two nanometres wide. The fibres can enhance the power of optical microscope. Silk from a spider of

Madagascar and another from the Middle East and South Asia is procured for the purpose.

If optical fibres are shrunk by about a thousand times, they can be used to probe living cells or etch nanoscale electronic circuits. The fibres will actually be nanowire lasers, made from semiconductors such as cadmium sulphide. In fact, the first nanowire lasers were made in 2001 from zinc oxide. Scientists have been able to switch lasers on and off. Lasers in silicon chips would further speed up progress in information technology.

IBM researchers have developed a technique to make the microscopic tubes emit light and have made a nanotube transistor that emits infrared light at a frequency generally used in telecommunications. It was found that the wavelength of light emitted is inversely proportional to the tube's diameter. The researchers have also generated electrical current in a single carbon nanotube by simply shining light on it. The achievement indicates that the nanotube can serve as a nanoscale photodetector. Optical fibres that are 50nm wide (some 2000 times finer than standard ones used in optical links today) have been made. Without any cladding that surrounds their inner core in a standard optical fibre, the thinner fibre can carry more of the wave across its surface. The fibres are indeed thinner than the wavelengths of light they carry.

A Green Remedy

A significant area of nanoresearch concerns the global environment. A simple innovation, if successfully adopted, would address the problem of global warming. Scientists have made artificial leaves that can inhale carbon dioxide even at night. This follows a unique discovery that some substances could act as a catalyst in transforming carbon dioxide into other organic molecules. Nanocrystals of a particular size with cadmium selenide could initiate the

reaction. If indium atoms are also added, not even light is required for the leaves to absorb carbon dioxide. Each carbon dioxide molecule, when attached to the metal, takes on an electron.

Meanwhile, scientists at the Cornell University (USA) have developed a microscopic device that derives power from nickel-63, a radioactive isotope, which has a half-life of over 100 years. (Half-life is the time it takes for half the atoms in an element to decay.) The power from the device can last for decades and can be used to run remote sensors or devices implanted in the body. Again, if the cost-benefit analysis would support the exploitation of the technique, it would be widely adopted.

Portable gas monitors are being developed with carbon nanotube-based sensors to detect gases for environmental, industrial and counter-terrorism applications. The presence of a gas on the surface of the nanotube would cause changes in its electrical conductance and thereby reveal a 'fingerprint'. A biosensor with gold nanoparticles would be able to detect both beneficial and toxic metal ions. Such a sensor could detect the presence of lead, mercury and other toxic ions. Nanosensors can be used to flush out metal ions from water as well as detect them in and out of human cells to better understand muscle contraction. The use of nanoporous polymers for water purification is also studied.

Another fundamental change is being envisaged. As technology improves, most of the farmland may not be required to meet the food needs of the world! A small per centage of the cultivable land would be adequate and there would thus be no need to destroy forests. This would be a blessing for developing countries. These are currently a wish list, though technological progress may spring a surprise and make it happen sooner than we now think. There is however a short-term concern. In the name of upgrading some crops, scientists may genetically modify or even

demolish crop variety, which has sustained them through the ages.

Nanoparticles of magnesium oxide have been found to be effective in the fight against bacteria. The particles have an electrical charge opposite to that of bacteria and so are attracted to them killing the bacteria in five minutes. The nanoparticles are not harmful to humans.

Chemists at the Bhabha Atomic Research Centre have taken up the synthesis and study of nanosized uranium oxide crystallites. The object is to explore the process for managing nuclear waste and study if the depleted uranium can be developed as a useful catalyst.

Environmentally benign nanocomposites and nanoparticles of titanium dioxide for cleansing the environment are also being developed.

Scientists at IIT, Kharagpur have found that silver nanoparticles could act as a catalyst in some chemicals to detect arsenic in water samples. The problem of underground water pollution is severe in parts of West Bengal. The scientists used ultraviolet radiation to synthesise tiny particles of silver and gold. The technique could detect arsenic even below the World Health Organization's permissible limit of 0.05 parts per million.

Nanomedicine: An Early Reality

The ongoing convergence of nanoelectronics and biology is a major development, which would profoundly affect all areas of life sciences and health care. Nanomedicine is no longer hype. Hundreds of companies are working in the areas of drug delivery, surgical aids and orthopaedic implants at the nanoscale. Work is also being done on magnetic nanoparticles that target molecules in tissues and cells.

The use of molecular motors as nanomachines and interfacing them with inorganic energy sources and other nanodevices would be of practical interest. Molecular

motors are responsible for DNA transcription, cellular transport and muscle contraction. The motors can be used as actuators. Organic chemists are synthesising molecules capable of different kinds of motors at the nanolevel.

DNA chips and arrays will be useful in diagnostics and genetic research. They are devices that generally have 100 to 1,00,000 different pixels (picture elements) for DNA sites on the chip surface. The arrays would be used in drug discovery, forensics and detection of information on diseases. Nanoparticles containing DNA may provide viable means of drug delivery and transfer of genetic materials. DNA microarrays can also be used in electronic and photonic devices. Semiconductor nanocrystals can serve as fluorescent biological labels. Detection of toxic substances can help in the fight against terrorists and polluters. Nanochips may soon be used to carry out a comprehensive chemical analysis. Ingestible nanodevices will revolutionise medical diagnostic.

Overdose of drugs has been a recurring problem. Nano-sized sponges have been found to remove any overdose of drugs from the bloodstream. Nanotubes with fats inside can dissolve drugs. The device would be in widespread use, as drugs affect the human body in many ways not yet fully known.

Scientists are trying to learn from Nature. Biological ion channels, for example, (measuring a few one-tenths of a nanometre), open and close, admit only specified ions, regulate heartbeat, and kill bacteria and cancer cells. Materials for filtering and trapping selected components are being developed; they would be useful in water treatment and cleaning up the environment.

At the Stanford University, an array of detectors has been created with single-walled nanotubes that could sense gases at very low concentration. For instance, a device can detect nitrogen dioxide concentration of about 10–50 parts

per billion. Ultra-sensitive detectors can soon spot molecules at low levels, viz. 100 parts per trillion.

A Nano Nose!

A nano nose is in the news. Gold-coated silicon bars—2 nm long and 50 nm thick—can catch molecules and reflect any extra weight resulting from it. It is claimed that usually small quantities can be weighed in terms of femto grams. Silicon bars, coated with different substances, can absorb particles such as chemical contaminants, DNA or proteins.

Nano barcoding has emerged as a useful tool for bioanalysis. Microrods with bar codes, coated with different reagents can capture biological molecules such as DNA sequences and proteins. With expanding research in genomics and proteomics, it would be necessary to measure and analyse samples (such as blood) simultaneously in very small volumes.

Scientists in Taiwan have made a semiconductor that can home in on tumour cells. It has a core of cadmium and selenium crystals wrapped in a zinc-sulphur compound. The structure can display different fluorescent colouring depending on its size. Its size can vary when it binds with other molecules. The device was able to target specific molecules on tumour cells. The fluorescent markers were made from 5 nm semiconductors. It is non-toxic and suitable for use in live cells.

Hailed as one of the cornerstones of real-time imaging, fluorescent probes have revealed the true state of live cells. This has helped cell biologists to understand many complex processes such as enzyme activation. High-speed nano-focus devices for scanning microscopes have been developed to measure the position of moving parts.

Embryonic Cells in Action

Researchers say that nanocrystals have shed their 'fear' of

water. They can therefore be used to image developing embryonic cells in unprecedented detail and in full colour over extended periods of time. Currently, imaging techniques use organic dyes. The inorganic semiconductor nanocrystals that are now used are known as quantum dots. They are nanometric crystals developed in the 1980s for opto-electronics applications. A significant feature of the dots is that their size could be precisely tuned during chemical synthesis and this gives them novel properties. Once inside the body, the crystals act as multicolour beacons for use in imagery. The dots re-emit light at a variety of wavelengths depending on the size of their core. For example, a 3 nm particle of cadmium selenide radiates green light. The success of the dot depends on whether it is soluble and whether it is non-toxic.

A Rockefeller team of scientists in the US has managed to put the dot in a chemical surrounded by a water-tolerant shell. The surface of the capsule has been chemically treated, so that it can stick to biological macromolecules including DNA.

In an experiment on a frog, researchers injected billions of quantum dots and imaged the embryonic cell development without any harm to the cell. The fluorescent particles could be seen even in the offspring of the parent injected with the dots. Further studies are being done to see if a large quantity is required for the dots to act effectively.

Back to Basics

Advances in the basic understanding of matter have led to the making of new materials. Verification of the theoretical limits is nowadays possible in computers before exploring new features in laboratories. This method minimises false leads and sharpens target-oriented research. Scientists have taken two basic steps for manipulating matter into tiny machines. One was making a glue that would help in forming thousands of nanoparticles into highly ordered

structures. As each particle could serve as a memory element, the ability to manipulate the particles has become important. And it is possible now to push around individual atoms and position them in the required places.

The nature of liquids and gases, called amorphous, is being studied at the atomic and molecular levels. A recent finding is that atoms and molecules in a liquid are quite organised. A better knowledge of the composition and structure of liquids and gases would enable chemists to tailor-make selected materials with desired properties.

A Matter of Size

Nanostructures combining ceramic and metallic materials are likely to create new generations of ultra strong materials, new types of ferromagnets, strong ductile cements and new biomedical prosthetics. Polymers reinforced with nanoparticles are likely to be used for automobile parts.

One of the best methods to demonstrate that size matters in the way a material behaves is the use of an ultra-thin film containing 1 nm thick clay particles. Clay minerals behave differently when they are in bulk form. When it has only one layer, a combination of organic molecules would result in new hybrid materials. Stronger and lighter plastics and better sensors to detect biological and chemical agents are some of the novel applications envisaged.

The new generation of microscopes has made a dramatic impact on the study of nanoparticles that may act as catalysts. Advances in computer processing of data revealed by the microscopes have made it possible to examine particles that are only a few atoms in size. Moreover, the ability to synthesise materials of the same size and shape has vastly expanded the scope for creating new catalyst particles. The relationship between structure and performance could now be understood at the molecular level.

The importance of catalysts, which are critical to

chemical reactions, is well known. Catalysts are essential for making thousands of products ranging from lubricants to cancer drugs. In addition, catalysts play a key role in reducing air and water pollution. The performance of catalyst particles is found to be sensitive to their shape and surface structure. Particles (about 1–50 nm in size) show physical and chemical properties that fall in between the smallest element and its bulk form. It is interesting to find that metal particles of 1–2 nm diameter would exhibit unexpected catalytic activity (e.g. gold particles).

Superconductivity

Nanotechnology has been utilised to achieve superconductivity (total absence of resistance in a conductor to the flow of electric current without any transmission loss) at room temperature. Superconductivity was discovered in mercury in 1911 at very low temperature and it was only in 1986 that two Swiss scientists discovered high-temperature superconductivity.

The unusual size and shape of the nanotubes have been found useful in making them superconductive at relatively high temperature (15 K). The exceptionally small size (only 4Å) of the carbon nanotubes endows them with strange electronic properties. Physicists at the Hong Kong University of Science and Technology have shown that it is possible to achieve higher superconducting temperature using carbon nanotubes of smaller diameter.

No More Oil in Power Politics?

In the near term, a clean-up of fossil fuel is likely to yield rich dividends. For example, if only an economical way can be found to remove sulphur from fossil fuels, it would make a big difference. This is not a distant dream; China's Shenhua Coal Company has produced diesel directly from coal using advances in nanocatalysis. Conventional catalysts, made in the last century, have been costly and time-consuming. Widespread use of novel catalysts could turn imports uneconomical. The United States has the world's largest recoverable coal resources and if only it develops the technology to derive diesel from coal in an economical way, that country's dependence on oil from abroad would decrease. Imagine a world where fossil oil is not needed as an energy source! Nanotechnology can remove oil from power politics.

Similarly, if synthetic wood is developed in a cost-effective manner, it could render logging precious natural forests unnecessary and even uneconomical. As an added bonus, pollution can be absorbed in the new technique by machines that work on command.

Fuel Cells: A New Deal

Nanotechnology is poised to play a key role in realising the goal of an economic and efficient fuel cell technology. The ideal fuel for the future is said to be hydrogen, due to its light weight and environmentally benign nature. If fuel cells were used in automobiles, air pollution would be reduced. But it can be used only if hydrogen is stored in a safe, efficient and economical way.

Nanotubes can store and release hydrogen. A nanotube structure that absorbs and releases hydrogen at low pressure has been developed at the University of Michigan. Japanese researchers have reported that nanostructured graphites could *adsorb* (hold molecules to the surface) hydrogen for storage operations at room temperature. Hydrogen *adsorption* by weight increased and the technique could be further developed. Hydrogen storage, however, continues to be a challenge. Currently, hydrogen adsorption by weight is around 4 per cent. Claims of even 6.5 per cent have proved difficult to emulate.

As different nanotube samples are used, results of

hydrogen retention in containers have not been uniform. Moreover, a carbon nanotube's properties themselves may change when exposed to surrounding gases such as hydrogen and oxygen. However, further research is under way and portable hydrogen storage systems could become practical and economic.

Efforts have been made to improve fuel efficiency. Nanotechnology could provide improved heat-resistant materials and enhance fuel efficiency in cars and aircraft. Engineers point out another advantage, viz. toughness on a nanoscale. Silica particles that are just 50 nm wide (100 times smaller than the width of a human hair) would greatly reduce the impact of a crack in the material. Conventional polymeric materials are too brittle to be used in engines; even if they are strengthened with graphite fibres, they are vulnerable (e.g. a bird hit can damage a plane's wing).

Solar Power

Special attention is given to using nanoparticles for solar power production. Many semiconductor materials were found to have the potential for use in solar power production, provided they are made into nanoparticles. As the properties of nanoparticles change with their size, nanoparticles of the right size can be made for solar cells. They would absorb all visible light, but nothing from the invisible light at the end of the visible spectrum. The latter would reduce the voltage obtained from solar cells. It is also suggested that reducing the material into nanoparticles could modify impurities in the silicon used in making solar cells. Indium selenide, for instance, has good potential for solar cells made of nanoparticles. Nanostructured photovoltaics could change the economic viability of renewable resources.

Plastics make poor photovoltaics. Out of a million photons that strike a plastic solar cell, only one produces electric current. Moreover, after a few hours, atmospheric

oxygen creeps in and spoils the game. However, if the polymer has a network of nanotubes, it would greatly strengthen solar cells in terms of their power production. Almost five per cent of light, it is claimed, could be converted into electricity. Nanotubes can make plastic solar cells convert sunlight into electricity 50,000 times more efficiently than conventional plastics.

Nanotubes can turn some plastics into efficient conductors of electricity and can replace copper. This could potentially minimise copper in an aircraft and make it lighter. Plastic transistors are also coming into use. A surface with a high absorption of solar radiation and low thermal emission would be ideal for solar energy collectors. Such a coating can be prepared biologically. Silver particles synthesised in certain bacteria have been found to possess a unique spectral coating useful for efficient solar energy collection.

In another attempt, high-efficiency solar cells with a layer of diamond are expected to generate 300 W of solar power for every square metre on the Earth. The fruition of this technology would radically change the pattern of power production and its costs.

Scientists at the National Physical Laboratory, New Delhi and the Department of Chemistry of the University of Delhi have taken up the study of cadmium telluride, an absorber material for solar cells. It is known for its efficient utilisation of solar energy.

Meanwhile, scientists have developed a microscopic device that derives power from a radioactive isotope. Again, if the cost-benefit analysis would support the exploitation of the technique, it would be widely adopted.

Current from Water

Perhaps the most startling news about generating electricity has emanated from Bangalore! All it takes to produce

electricity is a bundle of nanotubes stuck under a running water tap! It looks so simple but a lot of physics has gone into it (Box 14).

Box 14

Electricity from Tap Water

A team of scientists led by Prof. Ajay Sood of the Indian Institute of Science, Bangalore, has successfully done an experiment to prove that electricity can be generated from tap water using nanotubes. Prof. N. Kumar of the Raman Research Institute, Bangalore, provided the theoretical model for the experiment. Theoretical predictions about generating current from a fluid flowing on a nanotube were made by two foreign scientists, P. Kral and M. Shapiro of the Weizmann Institute of Science, Israel. But the Bangalore experiment showed that the results were different from their predictions.

In the experiment, the scientists attached electrodes to the top and bottom of a clump of single-walled nanotubes made in the laboratory of Prof. C.N.R. Rao and pumped water through the tubes with an average diameter of 1.5 nm and measured the voltage of the current. They found that even if the velocity of the water was as low as a millionth of a metre, millivolts of current was produced. The voltage was noted within a millisecond and was along the direction of the flow. If the water flow was increased, the voltage also increased and if the velocity became very high, then saturation resulted. The scientists found that the voltage also increased when they added hydrochloric acid to the water, thereby increasing the number of positive hydrogen ions in the water.

The experiment provided the basis for building a simple energy conversion device that can convert mechanical energy into electricity. Since the generated voltage was sensitive to the flow of the liquid, the result provides ground for building a flow sensor that can register very minute quantity of liquids. Such sensors can also be used in biological devices such as pace makers.

Learning from the Lotus

The lotus—the icon of purity—symbolises the emergence of the best even in the worst of environment. The flower and the plant could well serve as a symbol of a blooming nanotechnology. Admired by poets and philosophers for its bloom above muddy waters, the lotus has inspired a nanoscale innovation.

A botanist from the University of Bonn, Germany, Wilhelm Barthcott has explained why. He points out that the lotus leaves stay dry even in a heavy shower. Lotus plants, he says, have superhydrophobic surface, which simply lets water droplets roll off, if there is a slight slope in the leaf, picking up small particles of dirt. The leaf is coated with hydrophobic wax crystals of about 1 nm in diameter. This provides the nanostructure with self-cleaning attribute. The same technique can be applied to clean wood, paper, textiles, masonry and leather. As a result, self-cleaning roofs, shoes and clothes may be available. A German company is already developing a spray-on coating that mimics the lotus.

The idea of self-cleaning material has been demonstrated in another application. A catalyst in glass oxidises common kinds of dirt and converts them into soluble molecules. And the glass will spread the rainwater evenly on its surface (unlike the ordinary glass which retains droplets of water) and let it run off. Glass, with an ultra-thin coating, about 40 nm thick, based on titanium dioxide has been found to clean itself. The organic debris on the glass is broken down when the ultraviolet waves in sunlight react with a photoresist. A mixture of chemical materials is added to the glass while it is in molten state. The new glass is already in production.

Consumer Products

Nanotechnology is slowly stepping out of the laboratories

into the consumer market in the United States and elsewhere. New materials with greater strength, toughness and shape memory as well as new magnetic materials with optical properties are being developed. Some 40 products are already available in the United States. There is a growing confidence that literally anything could be improved upon with nano inputs. Nanostructures are wrapped around or linked to traditional synthetic fibres. Nano products that have started coming to the market include a new kind of fabrics, chemically protective gloves and masks, mixtures of carbon fibrils in a variety of polymers and components used in cars, hard drives, copying machines and imaging devices.

A new class of 'smart materials' is on the cards. They include clothes that would repel dust and retain their shape and wrinkle-free texture in all conditions and anti-reflecting eyeglasses. Fabrics woven with sensors would detect chemicals, receive satellite signals and perform other tasks. Wearable computers would show the location of the wearer.

Electric bulbs made from carbon nanotubes come on instantly, dim easily and do not contain toxic mercury vapour, unlike fluorescent lights. The nanotubes emit electrons, which strike a phosphor coating inside the glass bulb. However, the efficiency of the nanotube-based bulb needs to be vastly upgraded, if it has to become cost-effective. Meanwhile, it has been found that single-walled nanotubes can produce light when a current is passed through it. Earlier, the tubes needed laser light to start off. The new finding makes it possible to use them in ultra-small optoelectronics.

A nano-thermometer has also been developed. The measurement is shown by the height of a continuous, unidimensional column of liquid gallium inside a carbon nanotube. Gallium is used as it has one of the widest liquid ranges of any metal (29.78ºC–2,403ºC). Moreover, it maintains a low vapour pressure even at high temperature.

The thermometer could be used in a variety of micro-environments.

Super Steel

An improved variety of stainless steel has been developed based on nanoscale data. The new metal performs better than the common grade cast steel at high temperatures (200ºC) and resists mechanical fatigue. It has been found that if steel is laced with nanoparticles, then it can last at least 1,000 times longer than the conventional metal. The Steel Research Centre in Tsukuba (Japan), which has developed the improved variety, states that it would be useful for making turbine blades and boiler turbines. The products would be lighter and thinner.

Tackling Bird Hits

The danger posed to aircraft by bird hits may soon be a thing of the past. A new tough, heat-resistant composite may soon be used to ward off bird hits. A technique has been developed to create such a composite. The new material is three to four times tougher than conventional plastic. Today's polymeric materials are brittle though reinforced with graphite. The new composite would break down the impact into millions of bits of individual silicon particles. Scientists foresee that the composite will soon replace aluminium, steel and iron in cars and aircraft wings.

The Nano Age is bound to see what is described as smart materials that are programmable to behave in a predetermined manner. Nano-machines and nano-computers could be incorporated in materials and objects, endowing them with complex behaviour. For example, materials that remember their shape would provide dent-free bumpers to cars and parts to other objects, as the metal would return to its original shape after a hit.

Space applications and space travel would benefit from

the development of super strong and super light materials. Other spin-off benefits would include nano-whiskers that would just dust off stains on clothes.

The search for new materials and their unusual properties has attracted researchers from a wide range of sciences involving chemists, physicists, biologists and computer engineers. There would be many a surprise in store for the researchers. Even the raw materials of nano devices may spring from totally strange and unexpected sources (Box 15).

On the Battlefield

Nanotechnology is being applied to improve key military capabilities too. Researchers at MIT focus on six major areas, viz. detection of threat, bullet-proofing and other threat protection measures; enhanced human performance; real time automated medical treatment; and most importantly reduction of the weight-load of a soldier. In addressing the challenges in these areas, several novel ideas are being tried. New biomaterials and nano devices are under study. Some of the developments envisaged are: bullet-proof battle armour which will filter out chemical agents and toxins; a cream that would kill bacteria in a few minutes; near-invisible uniforms; protection from infrared signals; nanoscale sensors that detect a soldier's pulse rate, blood pressure and other signs; and synthetic muscles that could stiffen to work as a cast for an injured leg or arm; and reduction of the load carried by a soldier (now about 70 kg) by a third. In fact, the future theatre of war will have numerous nanosensors that will give a complete picture of the tactical battlefield. The rules of military strategy will change.

The ability of nanosensors to detect the presence of even a single molecule of selected chemicals is being developed. It is difficult to identify harmful particles immediately. In a subway, detection of a reported release of nerve gas has to be done within minutes. In a battlefield also there may be

Box 15

Diatom: Nature's Wonder Material

It is true that diatom is not a familiar word. But it is making news today in the nano world. Diatoms are single-cell shell algae, which are at the bottom of the food-chain. They are present in any environment that has light and moisture. Surprisingly, they form about one-fourth of the world's biomass. Scientists say that there are two lakhs of diatom species. What is amazing is that they grow into 3-D structures by themselves. The structures have amorphous and porous silica shells in a variety of shapes each with a unique design, extraordinarily beautiful. They could form the basis of a new manufacturing technique without the use of toxic chemicals and open a new branch of nanotechnology.

In an unusual experiment, Ken Sandhage of Ohio University soaked a diatom shell in magnesium and found that it had replaced the shell's silicon. In other words, scientists can have an organism that builds itself to a given structure but allows them to change its matter. The shells consist of nanoporous silica particles. Scientists hope to breed diatoms to get the shape of the shells they need. The cell cycle of diatoms is just one day and so they could double their number in 24 hours. Nature makes the shape of the shell, while humans could shape their content.

Diatoms would enable researchers to realise their dream of 'placing atoms where you want'. Will it resemble the replicator in the science fiction movie, *Star Trek* (the device that makes anything wished for) by simply assembling atoms? The machine in real life may not be the exact copy of the screen image but there is no doubt that diatoms would become the raw material for several nanoscale applications.

Several groups worldwide are working on diatom nanotechnology. The work is of interest to a wide range of experts from water pollution control to fossil analysis in search of oil. The application of diatoms in biosensors would be particularly significant. Functional proteins can be wrapped in diatom-like shells to protect them from the natural defence mechanism inside the human body.

some poison in the air slowly building up. It is known that some biological particles will glow faintly at certain frequencies of light when an ultraviolet laser is used. However, the development of an accurate detector continues to be a big challenge and nanotechnology is being used to solve these problems.

A portable version of a mass spectrometer, which does not need a magnet, has been developed. Silicon dust with very tiny perforations is sprinkled in the field or on a wall. Antibodies can be inserted into the tiny pores and they would latch on to viruses. But it takes at least 24 hours to analyse the virus caught. One suggestion is the use of DNA that would attach itself to the germ's genetic material, if it were ripped open. Yet another idea is the use of a flowering plant *(arabidopsis)* that could be made to glow green, if it senses a harmful substance!

Another important area of research is the development of quantum computer, which would give a billionfold increase in processing power by performing many different computations at the same time. This is a long-term goal and is expected to break secret codes.

As the Nano Age advances, a new generation of nano machines, totally unexpected, is likely to emerge. Who would have imagined, for instance, that plans to design a redundant communications network in case of nuclear war would result in the Internet? Though nano devices in the near future would target upgrades of known innovations, the long-term goals cannot be predicted. There is concern that humans may lose control of the world to nano robots or suffer from possible health hazards from nanoparticles (*see* Chapter 10).

Nanoelectronics will underpin many innovations in other disciplines as well. Individually, the experiments and initial results appear too small a step to make waves but they do represent a new wave of innovation (Box 16).

Box 16

Small Steps or a Giant Leap?

Away from the limelight, innovative young minds are at work at the frontiers of scientific and technological research in nanotechnology. Taken individually, the effort seems to have resulted in small steps on paths hardly explored before. The findings are necessarily tentative and often conditional. However, taken together, the small steps trace out a giant leap for nanotechnology. The benefits as well as the risks can easily be hyped. They say what matters is not the actual science or technology but what the public think what they are!

Still there is no false dawn. The light is real as could be seen from the following random samples below:

- Carbon nanotubes that replace silicon in transistors.
- Data storage using atoms as binary bits.
- Downsizing of computers to that of a grain of sand.
- Tweezers that can pick up objects 5000th of a millimeter across.
- Use of proteins such as apoferritin, which stores iron in nanomagnetic computer memory.
- Protein molecules that would read DNA quickly.
- DNA molecule that makes 'fuel' for moving a tiny engine 10,000 times smaller than a pinhead.
- A DNA-based mechanical device, a moving arm, which is a precursor of nano robots.
- A new type of microchip that can spot and cure cancer at a very early stage.
- Microtechnology to develop an early warning system for heart attacks.
- Ultrasensitive chemical sensors to spot minute traces of nerve gas or anthrax or any pollution.
- Battle tanks that change colour during combat operations.
- Fabrics that repel dust, stay ironed and sense the heat and protect the wearer.
- Light materials that are strong enough for use in space transport.
- Techniques to absorb greenhouse gases from the atmosphere.

Developed and advancing countries have made significant research and development investment in nanoscience and nanotechnology. New business opportunities are opening up and nanotechnology is likely to become the dominant industry in the near future. The world market for nano products is expected to grow to over US$ 1 trillion in the next ten years by 2015 from US$15 billion estimated for 2002.

Carbon Nanotubes: A Failure

Some observers have expressed their disappointment at the slow and often negative progress of the carbon nanotubes. The critics point out that carbon was the first structure to be discovered as a nanotube, but it is now yielding place to other materials.

The critics question the hype that sometimes surround the publicity about the nanotubes. It is pointed out that carbon nanotubes failed as a lubricant, did not resist the impact of a bullet on the clothing made out of it and burnt out easily.

Some researchers have turned to non-carbon nanotubes such as those made of tungsten and sulphur atoms. In another development, nanotubes made of titanium compounds have been found to be excellent detectors of hydrogen. Boron nitrade nanotubes have been found to be good semiconductors and what is more they need not be separated from metallic forms, as is the case with the carbon nanotubes.

However, it is too early to write off carbon nanotubes, as they conduct electricity very well.

Evolution Comes a Full Circle

What we are witnessing today is only a preview of the Nano Revolution. This is the first time in history that the nanoscale will measure the technological progress. Nanotechnology will affect almost every aspect of our lives. Basically the revolution aims at working on the same scale as nature.

Many scientists believe that life on Earth started on a nanoscale some 3.5 billion years ago. Evolution seems to be making a full circle. Once again, nanostructures and techniques would dominate but with a difference, viz. this time there is human intelligence. This difference is vital as it represents perhaps the only hope of humankind; it would enable humans to prevail over mindless machines as well as the minds, if any, of terrorists.

A Space Elevator

The fast pace of development of nanotechnology-based products has prompted futurists to envisage the realisation of some ideas that are just science fiction today. One such proposal is a space elevator to access the geosynchronous orbit, about 36,000 km above the equator. Communications satellites such as INSAT, HOT BIRD and INTELSAT are placed in this orbit. Currently, satellites designed for this orbit are launched by rockets such as geosynchronous satellite launch vehicle (GSLV).

The world-famous science writer, Arthur Clarke, who first proposed in 1945 the geosynchronous orbit even before the Space Age, himself envisages a space elevator to replace rockets in future. No one was then sure that such an orbit would become a reality in a matter of two decades. The use of the orbit envisaged by him has changed the way we inform and entertain ourselves and communicate with others across the world. Clarke has suggested that a cable for the elevator could be made of some strong material such as buckminsterfullerene. Nanotechnology is expected to provide the required material some day. Richard Smalley has commented that carbon nanotube was just the material for the space elevator.

One suggestion is to anchor such a cable to the surface of the Earth at one end and extend its other end all the way to a distant asteroid to provide extra stability. A less

ambitious goal would be to connect it to an object in orbit when required. Though these ideas are science fiction today, developments in nanomaterials may turn it into a practical achievement (Box 17).

> Box 17
>
> **Nanotechnology in Space**
>
> Carbon nanotubes would replace copper in computers used in future satellites. Copper's resistance to electricity increases as the metal's dimension decreases. Hence, copper is not suitable for nanoscale connections.
>
> The Centre for Nanotechnology of NASA Ames Research Centre has found that carbon nanotubes are quite suitable for interconnecting parts within integrated circuits. The tubes can conduct very high currents, more than a million amperes in one-centimeter square area. And there is no need to dig trenches to place the whisker-like nanotubes in the integrated circuits.
>
> Several other innovations are being tried by the Ames Center, which has 50 specialists. Some of the research findings could change the very economics of satellites and space exploration. For example, nanoelectronics is expected to lead to autonomous spacecraft. Ultra-small sensors, power sources, communications and navigation devices, and propulsion are likely to undergo a major change and result in cost-effective subsystems on satellites. New sensors that would monitor astronaut's health and safety would be developed. Micro-rovers and life detection systems would be designed for planetary exploration.
>
> The Indian Space Programme, being a dynamic adopter of state-of-the-art techniques, is likely to eventually incorporate cost-effective features of nanotechnology applicable to rockets and satellites. A nanosatellite is also envisaged as a possibility.

9

A BONANZA FOR TERRORISTS

I know only two things that are infinite—the universe, and human stupidity. And I'm not sure about the first.

—Albert Einstein

Nanotechnology empowers individuals to acquire the power to selectively destroy an area or a group of people. For the first time, the use of modern technology does not require large manufacturing facilities or rare raw materials. Knowledge will play a critical role and can lead to mass destruction.

Biological weapons include bacteria, viruses and toxins that can be released in the air or water. Over 20 varieties of bacteria, more than 40 viruses and 14 toxins are considered potential threats. Terrorists may grab drug-resistant strains as they are very effective, relatively cheap to produce, and easy to deploy. For example, a few grams of anthrax (fatal, if inhaled) put in envelopes could infect thousands of people, who open the mail.

Terrorists may well take advantage of genetic engineering techniques and misuse them. It is possible to develop anthrax, plague and tularemia (infectious disease leading to skin ulcers and pneumonia). The creation of strains such as these is denounced as black biology.

Hitherto, acquisition of chemical and biological weapons of mass destruction was a complex procedure. Today, thanks to the public databases on the Internet, it is almost

impossible to deny access to anyone including those hell-bent on acquiring the know-how for destruction. As if to illustrate this risk, two university students in New York made a polio virus from scratch in 2002! Details of the genetic sequences of many viruses are available on the Internet. It is often remarked that it is easier to make destructive use of a technology rather than use it constructively. This is doubly true of knowledge-based works.

New Weapons of Mass Destruction

Some experts have warned that nanotechnology would make it easy for terrorists to acquire nuclear weapons of mass destruction with very little fissionable material. The production of such weapons would not call for big uranium or plutonium plants. A few kilograms of deuterium-tritium mixture would be adequate to make the weapons. They can be precisely aimed without any elaborate launch facility, avoiding any radioactive fallout. The know-how for such weapons, it is feared, would be made available on the Internet. Individuals and small groups of terrorists would be empowered by the knowledge. This is considered to be a dangerous trend with no easy solutions.

A note of extreme caution has marked all research on bioweapon-related anti-terrorist strategy, especially in the United States after the September 11 terrorist attacks. For instance, Craig Venter, Head of Celera Genomics that collaborated in the Human Genome Project, found that it would be enough to have only 265 to 380 essential genes to grow a bacterium (called *Mycoplasma genitalium*), which happens to be the smallest replicating cell. The new knowledge empowers scientists to create an artificial bacterium. The project to grow the bacterium has been shelved until the ethical issues raised by it are resolved by leading scientists and other scholars. The safety aspect of such ventures has assumed considerable importance nowadays.

Detecting Biohazards

Nanotechnology can also be used to detect biohazards. Selected organic molecules placed on gold nanoparticles have been found to react to the presence of nerve gas, or biological contaminants. And the metal nanoparticles would indicate the biohazard through an electric charge. This is an example of a computer interface with the biological world.

In a recent development it was found that even if a semiconductor is dipped into low-purity metal salts or gold waste, the desired nanoparticles were obtained. This would avoid the need for pure gold (currently used). A research team of Purdue University has demonstrated this cost-effective way of forming tiny particles on the surface of semiconductors such as gallium arsenide in order to form a delicate interface between the microcircuits and the big wires that carry commands.

Another method exploits the human cell's reaction immediately on exposure to biological weapons. It has been found that the combinations of genes expressed in the reaction are unique to each biological agent. Some 50 genes seem to be adequate to indicate a pathogen. However, a new technology tests 40,000 genes per sample. An examination of gene expression would indicate the type of the biological weapon used. The analysis of the data is sophisticated enough to distinguish between different diseases. This is significant as the initial symptoms of anthrax and influenza, for example, are the same.

Detecting the Threat

Sophisticated techniques are under development to meet the threat of biological weapons. As timely detection of bioagents is critical in all these strategies, efforts to identify the dangerous elements focus on three basic techniques. One, detection of the DNA sequence unique to a bioagent; second, analysis of a sample through chemical mass

spectrometry; and three, study of the response in biological tissues hit by bioagents.

A highly sensitive and inexpensive 'lab-on-a-chip' has been developed in the US to provide a warning within seconds of even trace amounts of toxic chemicals in water. It is a mini chemical and biological analysis system. Agents of biological warfare can be detected through colours emanating from silicon or germanium quantum dots in light emitting diodes (LEDs).

The DNA sequence of a bioagent is identified by making multiple copies of it for tests. The pathogen is generally identified in less than 30 minutes. The second method relies on live tissues or biological reagents. Chemical mass spectroscopy breaks down a sample into its component amino acids for comparison with known bioagents.

It is pointed out that terrorists need not master nanotechnology. For example, they could easily poison food or water without nano substances. But where bio-weapons are used, detection of bio-agents needs nanotechnology-based sensors. The ever-expanding microbial genome databases now provide a list of all potential genes involved. It is thus easy to pick and choose the most lethal combinations.

As stated by the President of the Institute for Genomic Research in Maryland (US), terrorists are just a few mouse clicks away from a database where they could easily find the sequences of, say, the Ebola virus. Key sequences of many deadly microbes are already well known. Moreover, theft of critical data cannot be ruled out. For instance, lethal pig bacterium unintentionally created by researchers was reported stolen from a university laboratory in the US.

The worst aspect of misuse of bioagents is their immunity from control. By swapping DNA on a yeast genome, researchers have turned one specimen into another, undoing thousands of years of evolutionary change. Similarly,

biological agents may alter human behaviour or fertility. The two methods need a database of known bioagents. In the third method, the response of live cells to toxins is measured. Toxins carry no DNA. This method is still being developed.

The US Congress passed a legislation (after the attacks in September 2001) that would require US laboratories working with any microbes on a given list of human, animal and plant pathogens to be registered with the Federal Government. There is a growing demand to extend the control measures to research on the so-called safe germs. However, self-regulation by scientists themselves is preferred to control from outside. It is also felt in some quarters that without an open exchange of information, there would be no accountability.

There is an urgent need for initiating steps to prevent terrorists from acquiring dangerous secrets potentially useful in biological warfare. The International Committee of the Red Cross has called on governments and scientists to clamp down work that could lead to bioweapons. The Red Cross made a similar appeal against poison gases in 1918 (after the end of the First World War) and recently initiated a campaign against landmines. The signatories of the 1972 Biological Weapons Convention urge strict measures to enforce the treaty banning bioweapons. The Treaty bans developing, producing, stockpiling or acquiring biological weapons or their delivery systems. But there is no provision for enforcement. Sean Howard, Editor of *Disarmament Diplomacy*, is of the view that nanotechnology portends some very dangerous developments and so he favours an inner space version of the 1967 Outer Space Treaty banning weapons of mass destruction in space.

10

NANO? NO, THANKS!

We can't simply do our science and not worry about the ethical issues.

—Bill Joy (co-founder, Sun Microsystems)

Michael Crichton, author of *Jurassic Park,* recently wrote a new thriller, *Prey*. The science fiction was a bestseller even before its official release. The book explores the applications of nanotechnology and artificial intelligence. The thriller describes self-replicating super-small and super-smart robots running amok. No wonder, the terror of runaway nano robots or nanobots has a widespread appeal.

Some observers who review the progress of nanotechnology quip that Crichton may soon have to hit on something novel, as nanobots would not remain in the realm of science fiction for long. It is no longer a question of whether but when such a nanobot may rain havoc on a helpless world. Even as the timing of the doomsday is under debate, green movements and prominent personalities have said no to nanodevices as they fear fatal implications of just inhaling nanoparticles, terrorists or no terrorists.

On the other hand, the driving force behind the huge investments on nanotechnology is its promise of a different world without many of the negative developments that today degrade the quality of human life. Nanoscale machines, built atom-by-atom or molecule-by-molecule, will be programmed to construct other things. A general-purpose

molecular assembler, as envisaged by Drexler, can replicate itself. The result will be programmable smart machines with hardly any waste in production. Nanobots can build almost anything, though Drexler himself has since discounted this possibility.

Many scientists had imagined machines with a difference. In his book, *What is life?* (1944), Edwin Schrodinger described life in terms of molecular objects. It was before the transistor was invented. In the 1950s, John Von Neumann envisaged that molecules could be programmed to become self-replicatory. The idea remained a matter of curiosity. In 1959, Arthur Von Hippel talked of designing materials from the bottom-up. The same year, Richard Feynman described building objects atom-by-atom. The practical means to translate the ideas on machines and materials was not available in those days. The story became different after the dramatic development of integrated circuits. Rapid advances in genetics, nanotechnology and robotics have opened up new possibilities.

Nanotechnology has come up in time to prolong the operation of Moore's law, when the silicon technology is likely to hit a dead end after about a decade. The new field of nanotechnology is likely to see computers a million times as powerful as today's PCs. In another three decades, computer devices will increasingly get implanted into the human body. A stage would come when it would not be true to call us 'humans', what with several gadgets embedded inside. Genetic engineering too can spring a few surprises: new species of bacteria, plants and even viruses may pop up. Cloning may replace reproduction. Nanoscale molecular electronics would make life incredibly comfortable though regulated by computers. That is the bright side of the picture.

Yet the very comforts offered by nanotechnology may spell danger. For the more pervasive a technology becomes,

the more reliant would be its users due to the continuous availability of such technical gadgets. Could we now, for example, think of living without telephones? Given the proliferation of the so-called user-friendly gadgets for our daily chores, the possibility of a machine-run society (with little human intervention) may not remain science fiction for long. And the prospect, however remote, of humans losing control over machines has troubled people. In other words, the scenario would not be the rise and fall of nanobots but one of rise and rise of nanobots.

Bill Joy's Concern

Rapid advances in computers have prompted Bill Joy, co-founder and Chief Scientist of Sun Microsystems to sound a note of caution. Bill has played a key role in the creation of Internet technologies such as Java and Jini. In a thought-provoking article 'Why the future does not need us?', published in *Wired* magazine, Bill Joy warned that robotics, genetic engineering and nanotechnology would threaten to make humans an endangered species, unable to call the shots in the midst of superior robots. Bill Joy poses the question, "Should we not proceed with great caution?" He argues that the complexity of today's computing will, in the not too distant future, outgrow the human ability to manage it. He envisaged a world where electronic devices would control most of our activities.

Bill Joy thinks that the superintelligent robots would become immortal, as they would replicate without any control. The spread of the Internet would make it easy for terrorists to activate the robots. Whether by accident or design, our biosphere itself may be destroyed irrevocably, resulting in what Joy calls the 'gray goo' problem. Gray goo refers to a mass of small, destructive, self-replicating nanobots, which will wipe out all traces of life. The real danger lies, as explained by Bill Joy, in the possibility of the

replicating and evolving processes, so far confined to the natural world, entering the areas of human effort!

Bill Joy's fears are not imaginary, if one goes by the growing concern about genetically modified crops. Researchers in Israel found a certain enhanced fungus that killed off tomato and tobacco seedlings, which were not its targets. In short, there is no foolproof measure against mistakes in genetic engineering. It is somewhat chilling to imagine a real life scenario of an independent computer running on its own (as did HAL 9000 in the movie, *2001: A Space Odyssey*) that could be switched off only by cutting off the power, thereby losing almost every other service offered by the computer.

Asimov's Laws of Robotics

Can robots be ordered to function within reasonable limits? One is reminded of the ethical rules for robots given by the famous science writer, Isaac Asimov. In his popular book, *I, Robot* (1950), Asimov proposed his three laws of robotics, viz. one, a robot may not injure a human being or through inaction, allow a human being to come to harm; two, a robot must obey the order given to it by human beings, except where such orders would conflict with the First Law; and three, a robot must protect its own existence as long as such protection does not conflict with the First or Second law.

The basic assumption of Asimov is that the human input in designing a robot would preclude its destructive behaviour against human interests. The rise of terrorism in today's world nullifies Asimov's assumption of altruism governing robotic behaviour. A terrorist could set the robots to reach a point of no return on its destructive path and endow it with uncontrollable freedom to hit the targets of its choice. The manufacture and deployment of nanoscale devices can be done secretly, away from monitoring sensors. The real concern, according to some scientists, is that

molecular disassemblers (as against the constructive assemblers) could be made and set to destroy buildings cell by cell in a subtle manner.

What can be done to address the problem? Some have suggested that one solution could be to relinquish research and development (R&D) of nanotechnology altogether. Not all people agree. Considering the significant improvement in the living conditions that can flow from the constructive use of nanotechnology, it would be unwise to throw it away in panic. Moreover, if R&D is not allowed, nanotechnology would go underground and it would then be impossible to regulate it. The chances of the results of R&D getting into the hands of terrorists will increase. Even if nanobots can be overcome by human ingenuity, uncontrolled chemical chain reaction set off by terrorists cannot be ruled out. The very potential for abuse of this technology calls for research on its risks and benefits.

There is, however, a ray of hope. Some guidelines on R&D would be necessary. The rationale seems to be that terrorists would take the easy route and pluck the low-hanging fruits of the main line R&D effort rather than follow up with fundamental research. Hence, it would make sense to follow strict safeguards while carrying out R&D. For instance, a nonprofit organisation in the US, viz. Foresight Institute (in Palo Alto, California) founded by Eric Drexler, has proposed a set of draft guidelines to inform developers and manufacturers of molecular systems. The safeguards include insistence on absolute dependence on an artificial fuel source or components not found in nature; error detection systems and encryption and inability to replicate in an uncontrolled environment. The draft guidelines would be refined as and when new developments arise.

Two types of nanomachines are envisaged. One is a very small version of today's big machines with dimensions of only a few billionths of a metre. The other is a completely new robot, called molecular assembler by Eric Drexler, which would position atoms and molecules into previously planned creations. But Drexler has recently (2004) declared that self-replicating machines are not necessary for molecular nanotechnology.

Research by a professor in California has resulted in designs of wall-climbing creatures and a six-legged robot. Other robots try to mimic cockroaches in running and crawling like spiders. The description of the abilities of these machines and their targets shows that a robot with superhuman qualities is still several years away.

If atoms can be individually used in construction, then a new kind of molecules would be available. The remarkable feature of such 'nanites' is that they could be programmed to carry out specific jobs. The end device, according to Drexler's earlier view, can theoretically make anything. This scenario is now discounted. Even if such an assembler were to work like an enzyme, it needs a water base. If on the other hand, the assembler is not based on water, then its chemical base has yet to be discovered. While Drexler points out that nanodots need no enzymes on living cells, as they are fundamentally mechanical, 'positioned' on a nanoscale by computers, Prof. Richard E. Smalley insists that such an all-powerful mechanical assembler just can't operate, and a self-replicating nanobot cannot emerge.

Rude Shock

Those who scoffed at the idea of self-replicating nanobots in the near future were in for a rude shock recently. A German chemist, Gunter von Kiedrowski and his team at the University of Ruhr announced that they were about to make self-replicating objects, some nanometres thick as they could copy the chemical data in molecules that can assemble themselves. He said he copied the techniques of DNA in copying and self-assembly. This claim should be viewed in the

context of today's progress in molecular nanotechnology, which makes it possible to introduce new information into DNA molecules. Electronic circuits are also possible since DNA can conduct electricity. The German team and other scientists in California independently reported another achievement. They showed that it is not necessary to use enzymes that nature has provided for replicating the DNA. Still the process needed human intervention.

Drexler had endowed his assembler with superhuman powers; it can build bottom up almost anything. In an essay called *A Dialog on Dangers,* he outlined the concerns of developing nanotechnology. But several scientists are of the view that the 'molecular assembler' envisaged by Drexler is not likely to emerge in the near future. It is true that the total number of transistors on an integrated circuit will equal the number of neurons in the human brain (estimated at 10^{11}) by the end of this decade (2010). It is also argued that the number-crunching capacity of a human-made chip is vastly superior to a biological neural network. Again, it is pointed out that the human brain can never equal the processing speed of the machine, which provides numerous algorithms. But neurons, which are three-dimensional, interact with one another and function in parallel with others, thereby giving the human brain vastly superior powers not in terms of memory or calculations but in terms of judgment, imagination and motivation. The danger of nanobots turning themselves against human beings (even without the intervention of terrorists) need not be inevitable.

The reason is in the nature of the human brain itself. It is pointed out that humans are built from about 40,000 genes. Neuroscientists point out that this number is simply not enough to specify many of the synapses (about 10^{15}) in the brain. Hence, not all of human behaviour can be genetically controlled, even if robots take over. It follows that all human behaviour cannot be programmed. That is good news.

Danger from Nanoparticles

Even as the pace of using a wide variety of nanostructures and particles is picking up, there is concern that the nanotubes and nanoparticles may prove to be imminent dangers to human health and environment. An editorial in *Nature* states, 'No one is considering building nanobots that replicate by manipulating atoms one at a time'. Rather, the journal states that the danger may come from potential toxicity of nanoparticles being promoted as diagnostic tools.

It is pointed out that while many materials are harmless in their bulk form, they need not be so, when they are reduced to fine nanoparticles. Inhaling them during their production may harm the lungs. Experiments on rats have not given a clean chit to nanoparticles. At the NASA's Johnson Space Centre in Houston, mice, which were exposed to carbon nanofibres, developed lesions in their lungs and intestines. It is feared that even harmless compounds may turn out to be risky on a nanometre scale. Some observers have indicated that carbon nanotubes could worsen the environment instead of improving it. The spread of pollutants may increase if they get attached to the tubes. However, there is a contrary view that the pollutants would become neutralised. Green lobbyists and environmental activists would prefer to call for a pause in the production and application of nanotubes until the toxic effect, if any, could be fully ascertained.

Prof. Richard Smalley, co-inventor of fullerene, does not think of nanobots as a threat, as in his view self-replicating mechanical robots are simply not possible. However, he does not wish to take chances with nanoparticles, especially because carbon nanotubes are being mass-produced. His group has set up a separate enclosed area to work with nanotubes.

The Action Group on Erosion, Technology and Concentration (ETC), based in Winnipeg, Canada points out that there are no rules to regulate the use of nanoparticles in the

laboratory or outside. ETC has called for a worldwide ban on nanotech research. Some centres have started research on the impact of nanoparticles on the human body. ETC says synthetic nanoparticles could be toxic.

Greenpeace (UK) has in a report conceded that nanotechnology may not be after all harmful and has not therefore demanded a ban on its use. However, the report has voiced concern about the lack of regulation of nanoparticles. Though valuable benefits may flow from nanotechnology (such as clean energy), Greenpeace would like scientists to be proactive and address the concerns of the common people and frankly pinpoint the risks, if any, in the use of the technology.

The US Congress has called for more funds to support R&D to bring out the social, ethical and environmental impact of nanotechnology. The US Environment Protection Agency has requested the Centre for Biological and Environmental Nanotechnology at Rice University in Houston to articulate the concerns in this regard. The American Chemical Society heard a presentation that suggested caution in using nanoparticles. The concern is all the more because of the exciting possibilities of using nano devices inside the body for imaging and drug delivery, though researchers would have to satisfy themselves that there would not be any adverse reaction on the healthy tissues in the experiments. Further research is on to find out where and in what circumstances the use of nanomaterials would be risky.

Ethics Should Catch Up

Bill Joy is not alone in voicing the concern about the rapid spread of nanotechnology. Britain's Prince Charles has also expressed his concern that the worst-case scenario of what is called gray goo might come true. Nanobots may consume the entire planet. The editor of *Ecologist*, Zac Goldsmith, has

stated that with nanotechnology there is real room for discomfort. The British government thought it fit to refer the ethical and social implications of nanotechnology to a joint panel of experts of the Royal Society and the Royal Academy of Engineering for investigation. The panel has in its report (2004) found no need to ban nanotechnology research but called for more research on health-related aspects of the technology.

Besides the health risk question, the ethical aspect of the new technology has assumed importance. This is articulated in many questions:

- First, is it right and safe to develop nanotechnology without fully understanding its implications to human health? The headlong rush to pour venture capital into anything nano, carries with it a risk greater than possible economic loss. Will nanotechnology not be taken over by multinational companies silencing the dissident scientists?
- Second, observers have warned that in terms of general acceptance of nanotechnology it might go the way of genetically modified food crops and attract severe criticism. The introduction of nano products may be seen as one more attempt of the industrialised West to secure monopoly markets in the developing world.
- Third, will nanotechnology, which needs a lot of seed money to develop, become the patented right of developed countries and result in widening the digital divide? Will it be another form of technological and economical domination?
- Fourth, to what extent will the human freedom and right to privacy be affected and what would be the safeguards, if any, against discrimination in the name of uncertain scientific findings and how would they be enforced?
- Fifth, who will ring the alarm bells if nanobots start

playing havoc? Nanobots, the prototypes of which are seen today in costly gimmicks may suddenly become a factor to reckon with in the name of progress.

- Finally, how can nanotechnology be kept away from terrorists who can easily acquire it?

While a well-informed public debate is called for by these questions, several scientists feel that it is not prudent to slow down the research and development of nanotechnology or its applications that have clear and undoubted benefits and carry effective safeguards against misuse. At the same time, it would be unrealistic to assume that nanobots could defy the special physics and chemistry of the nanoworld evolved by Nature.

Human Brain, Not a Pre-set Blueprint

If your house design states 'doorwaberogorwinstairver' (!), you would be perplexed and wonder what it is all about. Some people think of the recently sequenced human genome in similar terms. If it is a 'blueprint' of life, then it needs a lot of annotations. We are far from understanding how the vast number of bases indicated by the genome is transferred into a cell. As Stanley Fields, Professor of Genome Science at the University of Washington (Seattle, USA), who has used the genetic strategies of yeast to understand human protein functions and diseases, says, "Deciphering how a mere 10^7 nucleotides result in a yeast cell—let alone how $3x10^9$ nucleotides result in Tiger Woods (golf champion)—cannot begin until the genes have been annotated". This step includes figuring out the proteins that these genes encode. Understanding how all of these proteins collaborate to carry out cellular processes is the real enterprise at hand.

The big question now is how the genome is expressed and how the cell functions. Research is now focused on the non-genomic information passed on by a cell to its progeny, particularly to find out the factors that control gene expression. Using electron microscopy, biologists are trying to find out how the individual proteins form their working pattern. One finding that is emerging is that the proteins do not work alone; they form complexes for carrying out many important cellular functions. More than 200 protein complexes in yeast have been identified.

Even as the complexity of the human gene is being explored, there is a growing realisation that genes alone do not determine a person's character or behaviour. Ironically, there are some who view human nature as determined by genes only. For example, Prof. Francis Fukayama at Johns Hopkins University (USA) and author of *Our Post-human Future,* defines human nature as the sum of the behaviour and characteristics that are typical of the human species arising from genetic rather than environmental factors. Contrary to this view, many others have pointed out that the human nature is a whole, which is greater than the sum of its parts. Environment and circumstances of growth do contribute to the so-called essence of human nature.

The well-known science writer, Matt Ridley, in his recent book, *Nature via Nurture,* points out that it is no longer true to speak of Nature versus nurture, as the two are inextricably linked. While the encoded sequence of a gene is fixed and cannot be changed, the *expression* of the sequence is open to change by one's experience.

To sum up, human behaviour cannot fully be explained by pre-set hard wiring of the brain. The interconnections in the brain are not pre-set but are shaped by experience. In other words, DNA cannot be the undisputed ruler! The human mind tends to travel on ever-new paths with no specific destination. This exercise has benefited humankind in terms of unexpected benefits from innovations and new ideas. An initial first strike by robots may catch people unawares, but finally the brain's neural mechanism working in

parallel would defeat the machine. Ultimately, our intuition and imagination as well as a sense of values are the best safeguards against the victory of mindless robots. It would therefore be unrealistic to deny or delay the next revolution based on nanotechnology, provided an ever-vigilant scientific community is encouraged to give timely warning against possible risk or misuse.

Glossary

Angstrom: A unit of measurement indicating one-tenth of a nanometer (Å).

Antibody: A protein produced by B-cells (white blood cells) of the immune system.

Atomic force microscope (AFM): Does not use light but measures the force between atoms in the sample used for high-resolution imaging of molecules such as proteins and DNA.

Band gap: The gap in semiconductors between valence band (where electrons do not conduct electricity) and the conduction band.

Bose-Einstein condensate: A new form of matter, neither vaporous, nor hard, nor fluid.

Bottom up: Building larger objects from smaller building blocks (mostly done by chemists); construction of machines using atoms and molecules.

Buckminsterfullerene: A variety of buckyballs and carbon nanotubes. Named after the architect, Buckminsterfuller, famous for designing geodesic dome.

Buckytube: Cluster of C60 atoms.

Buckyball: Made of 60 carbon atoms, arranged in hexagonal shapes like a soccer ball.

Carbon nanotube: A cylinder-shaped structure resembling a rolled-up sheet of graphite.

Casimir effect: Force between objects in a vacuum, named after its discoverer, Hendrik Casimir.

Conductor: An object through which electricity can flow without much resistance.

Chemical vapour deposition: A technique used to deposit chemical coatings; chemicals are first vapourised and then applied using an inert carrier gas such as nitrogen.

Chromosome: A set of DNA with proteins inside the cell nucleus, storing genetic information.

DNA: Deoxyribonucleic acid. A molecule that contains genetic information.

Dendrimer: Synthetic, three-dimensional macromolecules formed using a nanoscale process. Greek word for 'tree', a polymer with branching parts.

Diatoms: Single-cell shell algae which are at the bottom of the food-chain.

Dip pen nanolithography: The process of fabricating one molecule-thick nanostructures on solid structures using an atomic force microscope.

Femtosecond: One quadrillionth of a second. It is to a second what a second is to 32,700,000 years.

Fullerene: A third form of carbon, after diamond and graphite.

Fluorescence: Emission of electromagnetic radiation caused by the flow of some form of energy into the emitting body.

Gene: Denotes a DNA segment. The same segment may belong to two or even three genes at the same time.

Genome: The entire genetic information of a living being that contains coded instructions for the growth and functioning of a living being.

Gray goo: A mass of destructive nanobots, credited with the capacity to wipe out all life.

Lithography (e.g. circuit): The process of copying a feature onto a surface using light, electron beams or X-rays.

Heisenberg uncertainty principle: The more precisely the position of an object is determined, the less precisely its *momentum* is known.

Human genome project: An international project (begun in 1990) to identify the complete sequence of the human genome (almost completed in 2003).

MEMS: Micro Electronic Mechanical System used to integrate various electromechanical functions on to integrated circuits.

Micrometre: A unit of measurement; one millionth of metre.

Molecular electronics: Any system with atomically precise electronic devices of nanometer dimension, especially if made of discrete molecular parts.

Nanites: Machines with atom-sized components.

Nano: Indicates one-billionth of something.

Nanoarray: An ultra-miniaturised array for biomolecular analysis.

Nanoassembler: Once it is perfected, anything could be built.

Nanobots: Small self-replicating nanorobots.

Nanocrystals: Nanoscale semiconductor crystals, typically about 10 nm in diameter.

Nanorods: Formed from multi-walled carbon nanotubes.

Nanoscale: 1–100 nm range.

Nanotube: Can act as conductor of electricity or semiconductor, depending on the direction in which the tubes appear to have been rolled.

Nucleic acids: DNA and RNA.

Orbital tower: An imagined cable that would serve as a space elevator between the Earth and the geosynchronous orbit.

Paradigm shift: A new conceptual world view replacing the traditional view (e.g. when Aryabhatta or Copernicus proposed the sun-centric theory instead of the geocentric notion).

Photolithography: A process for imprinting a circuit on a semiconductor by photographing the image onto a photosensitive substrate and etching away unwanted portion.

Photonic crystals: Photonic analogue of semiconductors that precisely steer light beams to the required spots.

PCR (polymerase chain reaction): A technique that makes it possible to amplify selected pieces of DNA.

Phage: Abbreviation for bacteriophage, which is a virus that kills a bacterium.

Photonic crystals: Devices in which a regular array of tiny holes or other features are patterned into a material that will steer light beams exactly where they are meant to go.

Pico: Trillionth of a meter (smaller than nano).

Proteomics: Refers to all the proteins expressed by a genome.

Polymer: A chemical compound representing a chain of recurring groups (e.g. polyethylene).

Quantum cascade laser: Laser that operates in the mid-to-far infrared region, used in high-precision spectroscopy.

Quantum computer: A computer based on quantum bits that can represent potentially any combination of *one* and *zero*.

Quantum dots: Nanometer-sized semiconductor crystals. Addition or deletion of a single electron results in a significant change in its property.

Qubit: Unlike conventional bits, a qubit can be both 1 and 0 at the same time.

Raman effect: A phenomenon observed in the scattering of light as it passes through a transparent medium.

Raman spectrum: A display of the intensity of Raman scattering of monochromatic light as a function of frequency of the scattered light.

Refraction: A measure of the speed of light in each material.

RNA: Ribonucleic acid. Transmits information from DNA to protein.

Scanning tunnelling microscope: A machine that reveals the atomic structure of particles; uses beams of electrons (not light) to scan the surface of a cell.

Self-assembly: Result of random motion of molecules and the affinity of their binding sites for one another.

Single-nucleotide polymorphism: Areas where the DNA sequence varies from person to person by a single genetic letter.

Spectroscopy: The physics related to the production, measurement and interpretation of electromagnetic spectra from emission or absorption of radiant energy by matter.

Spectrum: The set of frequencies, wavelengths or released quantities. Each element has a unique spectrum for emission and absorption of light.

Spintronics: Electronics based on the electron's spin-up and spin-down positions to indicate the *ones* and *zeros* of digital programming.

Semiconductor: A substance such as silicon, which conducts electricity under certain circumstances.

Superconductor: A material through which electricity is conducted without any resistance.

Terahertz radiation: Frequency of about a trillion waves a second from the area between light and radio waves in the electromagnetic spectrum.

Top-down: The building of small objects using larger items.

Virus: A cellular parasite. After it enters a cell, the latter switches its resources on to synthesise the nucleic acid and proteins of the virus.

Wavelength of light: 380 nm.

Wet nanotechnology: Study of biological systems that exist primarily in a water environment (e.g. genetic material).

X-ray crystallography: A technique of determining the internal structure of crystalline substances by special processing of the X-ray pattern resulting from them.

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